TEXTBOOK OF BRITISH SURGERY

Edited by

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VOLUME THREE: GENITO-URINARY SURGERY—PERIPHERAL VASCULAR DISEASES—PLASTIC SURGERY—ACTINOMYCOSIS—SURGERY IN THE TROPICS—VENEREAL AND ALLIED DISEASES — RADIOLOGY AND RADIOTHERAPY—SURGERY OF THE ADRENAL AND PARATHYROID GLANDS—BLOOD TRANSFUSION—FLUIDS AND ELECTROLYTES—HÆMORRHAGE—CHEMOTHERAPY



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GENERAL PREFACE

This volume of the *Textbook of British Surgery* covers Genito-Urinary Surgery—Peripheral Vascular Diseases—Plastic Surgery—Actinomycosis—Surgery in the Tropics—Venereal Diseases—Radiology and Radiotherapy—Surgery of the Adrenal and Parathyroid Glands—Blood Transfusion—Fluids and Electrolytes—Hæmorrhage—Shock and Chemotherapy, discussing fully diagnosis, pathology, prognosis and treatment of the areas concerned.

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The volume is essentially clinical and practical, with such pathology as is necessary for diagnosis and treatment. Surgical procedures are described, and the authors discuss the advantages and disadvantages of each procedure in vogue, indicating their reasons for preferring one to another.

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CHAPTER 1

GENITO-URINARY SURGERY

A. W. Badenoch

INVESTIGATIONS IN UROLOGY

In the majority of cases of disease of the genito-urinary system the diagnosis can be accurately established and the correct line of treatment can be planned before actual surgical intervention. This is due to the accuracy of special investigations which can be made, and these are done in three main ways (1) by laboratory investigations, (2) by radiological examination, and (3) by instrumentation and endoscopy of the urethra and bladder.

(1) Laboratory Investigations

Much can be learned from the examination of a freshly passed specimen of urine. When it is crystal clear and does not contain albumen there is no infection nor any hæmaturia at that particular time. If the colour is very pale, there is either a high fluid intake or poor renal function. If it is cloudy there may be a precipitation of phosphates. If the latter is the cause, a few drops of acetic acid will dissolve the phosphates and produce a crystal clear urine. If despite this addition, the cloudiness remains then it is due to either pus or bacteria or red cells. These will be seen and differentiated by microscopic examination of a centrifuged deposit and if infection is present, culture of the urine must be made and the infecting organism be distinguished.

Tests of Renal Function. If surgical disease of the kidney is confined to one side the other kidney will compensate for its inactive partner and there will be little or no appreciable diminution of overall function. If disease of the lower urinary tract is producing obstruction, however, both kidneys will be affected and total renal function will be depressed. Estimation of the degree of impairment is most important in assessing the risk of operation, in planning the scope of surgical intervention, and in indicating the best ancillary treatment before, during, and after operation. It is believed that inulin and creatinine are excreted through the glomeruli by filtration, and that diodone and certain other iodine compounds are excreted by the tubules. Tests have been evolved with a view to demonstrating which particular part of the nephron has been affected by disease, but these tests are at present largely academical and are as yet not of practical value in assessing the state of renal function in the presence of surgical disease.

Estimation of the urea concentration, of the total urea excretion, and of the urea clearance have all been used to determine this function. In unilateral disease the good kidney will produce a satisfactory test and so the result gives no indication of the degree of impairment on the affected side. It is in obstructive disease of the lower urinary tract that accurate estimation of the renal function is of great importance. The above tests require the bladder to be completely emptied at stated times. This necessitates the use of an indwelling urethral catheter which is undesirable, and such tests are therefore

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unsatisfactory. The estimation of the blood urea on the other hand, is of great value. This is normally between 20 and 40 mg. per 100 ml. and a figure much above the upper limit usually indicates considerable impairment of total kidney function. In children, where metabolism is more active, and in the elderly, the blood urea is often a little higher and may be about 50 mg. per 100 ml. In some gastro-intestinal lesions, such as are accompanied by severe vomiting, diarrhœa, or hæmatemesis the blood urea is usually raised, and it is also higher in the presence of a failing circulation from a decompensated heart.

The Estimation of the Blood Chlorides. The normal reading is 560–620 mg. per 100 ml. (96–106 m.eq). The output of chlorides is largely dependent on diet and if the intake is diminished so also will be the output. There is marked fall in output with excessive vomiting and diarrhœa. As the tissue sodium becomes depleted, non-protein nitrogen is retained to maintain the osmotic pressure. Hyperchloræmia occurs after uretero-colic anastomosis, when it is due in part at least, to re-absorption through the mucous membrane of the rectal wall.

The Estimation of the Alkali Reserve or Plasma Bicarbonate. This is the volume of CO_2 measured at normal temperature and pressure, which is expelled by acid from 100 vol. of plasma which has been equilibrated with normal alveolar air. It varies from 53–77 ml. of CO_2 per 100 ml. of plasma (24–34 m.eq). The pH of the blood has to be kept constantly between 7·3 and 7·5 and any redistribution of acid radicles relative to basic produces either acidosis or alkalosis. Acidosis occurs in diabetes mellitus, and if there is an excessive intake of acid. It is seen when there is a failure of phosphatic excretion, such as occurs in renal dwarfism associated with lower urinary obstruction, and may occur in gross bilateral hydronephrosis and in congenital polycystic disease. Alkalosis occurs when there is severe loss of acid or chlorides as with excessive vomiting, or when too much alkali has been administered. Renal damage results, and alkalæmia albumen and casts appear in the urine.

The Estimation of Plasma Proteins. The proteins total 5·6–8·5 per cent with albumen 4–6·7 and globulin 1·2–2·9. If the percentages fall below this, œdema occurs from renal failure and this estimation may be of considerable help in ascertaining the cause of œdema when it may be due either to a failing heart, to mechanical obstruction of the veins, or to renal dysfunction.

The Estimation of Serum Calcium and Serum Phosphorus. The normal serum calcium is 10 mg. per 100 ml. with a margin of + or — 1 mg. The normal adult serum phosphorus is 3 2 mg. per 100 ml. with a margin of + or — 0·5 mg In growing children and adolescents this figure may be as much as 1·2 mg. higher.

The Estimation of Serum Potassium. 15–22 mg./100 ml. (3·9–5·6 m eq). This may be of considerable importance in certain types of uræmia, more especially in that following uretero-colic anastomosis when the content is often lowered. This is not always constant and it is thought that the intra-cellular potassium may be diminished even though the serum potassium remains within normal limits. It has been suggested that in these cases certain alterations in the electrocardiographic findings may be more indicative of lowering of the potassium than is the biochemical estimation, but this is not generally accepted.

The Estimation of Hæmoglobin and Blood Count. This is of importance when hæmaturia has persisted or where an extensive radical operation is contemplated. Secondary anæmia is of common occurrence in chronic uræmia.

Radiological Examination of the Urinary Tract

In the diagnosis of surgical disease of the kidney, X-ray examination is essential and it is also of considerable help in elucidating the pathology and in the assessment of the best treatment of many disorders of the bladder and lower urinary tract. A plain or survey X-ray may show an opaque shadow suggestive of urinary calculus or other foreign body. In the kidney region on the right side, the differential diagnosis includes stone in the gall bladder or biliary tract, calcified mesenteric glands, calcification in blood vessels, especially the signet ring appearance sometimes seen in renal or splenic aneurism, calcification in costal cartilages, and foreign bodies in the bowel In the pelvic region a calculus must be differentiated from a phlebolith, which is calcification in a vein either of the lateral pelvic wall or in the wall of the bladder. A *calcified gland* as a rule has a fairly typical appearance: it has rather an irregular margin and its substance is fragmented. Usually there is more than one shadow present and the commonest situation is in the region of the right sacro iliac joint, in the situation of the route of the mesentery. A *phlebolith* is clear cut, oval or circular, with the edge rather denser than the centre There is nearly always more than one phlebolith and they are fairly constant in their position running down on each side of the bony pelvis If the patient is not unduly fat, the kidney outline can usually be seen on the plain view, its size and shape being both demonstrable. Enlargement may be seen in this view as may the shadow of a cyst or neoplasm, and the position of the lower pole approximating to the mid line will suggest congenital fusion.

Pyelography. Pyelography is most important. This may be either descending, following an intravenous injection, or ascending following the passage of a ureteric catheter along the ureter The outline of the renal pelvis and calyces is then demonstrated, also the line of the ureters. Intravenous pyelogram will show the function of each kidney and in most cases is an adequate investigation Retrograde pyelogram, on the other hand, shows up the outline of the calyces and pelves with far greater detail and is essential if the cause of hæmaturia cannot be demonstrated by an intravenous examination. The delineation of the pelves and calyces may be shown up in greater detail in an intravenous pyelogram, if pressure is applied over the lower third of the ureter. In performing a retrograde pyelogram, the opaque solution is injected along the ureter; in the first instance, 5 ml. of fluid is injected and the picture is taken. When possible it is advisable to perform this investigation under local anæsthesia as the patient can then tell if the pelvis is being overfilled.

Ureterography. The line and shape of the ureter is frequently seen after an intravenous pyelogram. This examination may be of prime importance to demonstrate whether or not an opaque shadow is in the line of the ureter. Usually it is necessary to pass a ureteric catheter and to take a picture either with or without an injection of dye. Retrograde ureterograms will demonstrate the degree of a hydro-ureter and may help in the diagnosis of a neoplasm of the ureter

Cystography. This can usually be performed as part of an excretion urography. It will demonstrate the size and shape of the bladder and may indicate the presence of a neoplasm, of trabeculation from obstruction, and the presence of a diverticulum (*see* Fig. 1). It will show the irritability of the bladder and the diminished capacity in a tuberculosis infection; it may show a filling defect from enlargement of the prostate, or a [illegible]nel neck from a neurological disorder.

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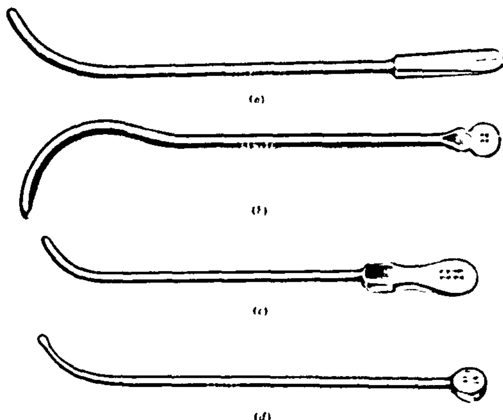
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metal and are arranged in graduated sets. For their proper use, it is essential that a complete series should be available. There are several scales or graduations of urethral instruments. In France and other parts of the Continent, the gauge generally used is the Béniqué scale, in which each instrument increases in diameter by one-sixth of a millimetre. In this country, and America, the Charrière scale which is also known as the French



(a)

(b)

(c)

(d)

Fig. 2 Metal bougies
(a) Buckston-Browne
(b) Béniqué
(c) Clutton
(d) Lister

scale is much more often employed and is twice the size of the Béniqué, the series increasing in diameter by one-third of a millimetre. In Britain, in India, and in South America, a large number of instruments are measured in the English scale. This is not really a satisfactory grading as it increases too rapidly in size, and therefore does not allow for accuracy in small instruments. For this reason and furthermore, since the gauge is rather arbitrary, it should be discarded. Metal bougies are curved for a variable distance of 3–5 cm before the tip and most types have some degree of tapering usually through four Charrière sizes. The commonest designs are those of Buckston-Browne, Clutton, Lister, and Béniqué (*see* Fig. 2). The Clutton sound which curves nearest to the tip is the simplest to use for stricture of the bulbous urethra. The Béniqué has a double curve and is of advantage in obstruction of the neck of the bladder. Straight sounds, Wyndham-Powell, are used to dilate the external urinary meatus, and for strictures of the penile urethra. Larger sizes of this pattern are useful to dilate a suprapubic fistula when the tube has accidentally come out and cannot easily be reintroduced.

Urethrography. This may be of importance and is usually done by the retrograde method. It is often more practicable to use the oily solution of lipiodol rather than a watery solution such as of diodone. Care must be taken not to use much pressure in injecting this along the urethra as some may be forced into the vascular spaces of the erectile tissue and embolism from this has been reported. The examination is of importance in demonstrating the length of a stricture, prior to operation, or in showing the



Fig. 1 After emptying bladder, the residual urine Note—the trabeculation of the bladder along with the wide neck of the diverticulum.

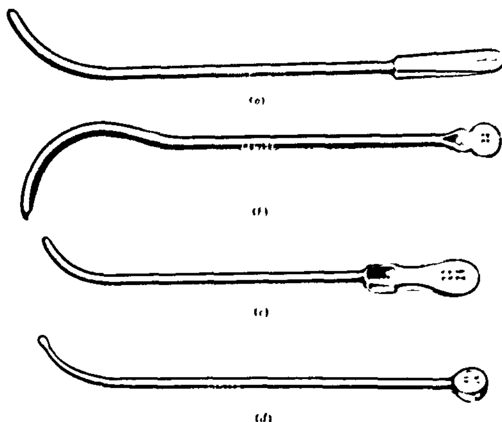
presence of a neoplasm of the urethra. A urethrogram taken during micturition may show prostatic crypts indicating chronic prostatitis.

Aortography and Renal Arteriography. Iodine compounds have been injected directly into the aorta and the renal arteries and their branches have been demonstrated. This investigation has not so far proved to be of wide practical value except in one or two special instances. It may be helpful where a space-filling tumour, either solid or cystic, is seen on pyelogram. If it is a neoplasm there will be a marked increase in the vascularity and "laking," whilst if due to a cyst there is much diminution in the arterial trees running to it. This examination is also worth doing in a non-functioning kidney even when there does not appear to be a ureteric orifice on this side. It may demonstrate an ectopic kidney and may be of much help in showing the exact arterial supply prior to partial nephrectomy or in a horseshoe kidney, should division be contemplated.

Instrumentation of the Urethra. The instruments which are passed along the urethra are of various types; sounds or bougies are solid, catheters are hollow, and endoscopic instruments carry a light and telescope

Bougies or Sounds. These may be made of gum-elastic web, of plastic material or of

metal and are arranged in graduated sets For their proper use, it is essential that a complete series should be available. There are several scales or graduations of urethral instruments In France and other parts of the Continent, the gauge generally used is the Béniqué scale, in which each instrument increases in diameter by one-sixth of a millimetre In this country, and America, the Charrière scale which is also known as the French



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(d) Lister

scale is much more often employed and is twice the size of the Béniqué, the series increasing in diameter by one-third of a millimetre In Britain, in India, and in South America, a large number of instruments are measured in the English scale. This is not really a satisfactory grading as it increases too rapidly in size, and therefore does not allow for accuracy in small instruments For this reason and furthermore, since the gauge is rather arbitrary, it should be discarded Metal bougies are curved for a variable distance of 3–5 cm before the tip and most types have some degree of tapering usually through four Charrière sizes The commonest designs are those of Buckston-Browne, Clutton, Lister, and Béniqué (*see* Fig 2) The Clutton sound which curves nearest to the tip is the simplest to use for stricture of the bulbous urethra. The Béniqué has a double curve and is of advantage in obstruction of the neck of the bladder. Straight sounds, Wyndham-Powell, are used to dilate the external urinary meatus, and for strictures of the penile urethra Larger sizes of this pattern are useful to dilate a suprapubic fistula when the tube has accidentally come out and cannot easily be reintroduced.

Urethrography. This may be of importance and is usually done by the retrograde method. It is often more practicable to use the oily solution of lipiodol rather than a watery solution such as of diodone. Care must be taken not to use much pressure in injecting this along the urethra as some may be forced into the vascular spaces of the erectile tissue and embolism from this has been reported. The examination is of importance in demonstrating the length of a stricture, prior to operation, or in showing the



FIG 1 After emptying bladder, the residual urine Note—the trabeculation of the bladder along with the wide neck of the diverticulum

presence of a neoplasm of the urethra. A urethrogram taken during micturition may show prostatic crypts indicating chronic prostatitis.

Aortography and Renal Arteriography. Iodine compounds have been injected directly into the aorta and the renal arteries and their branches have been demonstrated. This investigation has not so far proved to be of wide practical value except in one or two special instances It may be helpful where a space-filling tumour, either solid or cystic, is seen on pyelogram. If it is a neoplasm there will be a marked increase in the vascularity and "laking," whilst if due to a cyst there is much diminution in the arterial trees running to it. This examination is also worth doing in a non-functioning kidney even when there does not appear to be a ureteric orifice on this side. It may demonstrate an ectopic kidney and may be of much help in showing the exact arterial supply prior to partial nephrectomy or in a horseshoe kidney, should division be contemplated.

Instrumentation of the Urethra. The instruments which are passed along the urethra are of various types, sounds or bougies are solid, catheters are hollow, and endoscopic instruments carry a light and telescope.

Bougies or Sounds. These may be made of gum-elastic web, of plastic material or of

instrument (see Fig. 6). It is made of latex rubber, which is rather less irritating to the mucous membrane and carries a small balloon at the bladder end which can be inflated with water through a secondary channel. Catheters may be obtained with balloons of different sizes, a 5 ml. being satisfactory for self-retention. Gum-elastic instruments are

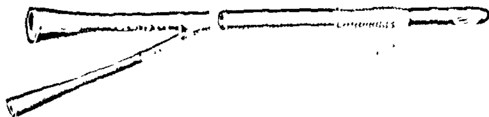


Fig. 6. Foley catheter



(a)



(b)



(c)

Fig. 7. Gum-elastic catheters
(a) Olivary tipped
(b) Coudé
(c) Bi-coudé

much less commonly used than they used to be. There are three main types, olivary tipped, coudé and bi-coudé (*see* Fig. 7). The olivary tipped instrument is especially suitable for passing through a stricture of the urethra; the coudé and bi-coudé can occasionally be passed in enlargement of the prostate when a Tiemann's has failed. Gum-elastic instruments can be sterilized by boiling, only when great care is exercised. If tied in the urethra, the gum may perish and fragments are apt to remain in the bladder or in the urethra. Plastic instruments, of more *recent design*, may ultimately replace those made from other materials. Metal catheters occasionally have to be used in stricture of the urethra or after post-prostatectomy obstruction.

Anæsthetization of the Urethra. The correct selection of instruments, skill of the operator, and gentleness are probably the most effective contributions to comfort *in*

Catheters. These are of many shapes and may be made of rubber, gum-elastic web, plastic, or metal (*see* Figs. 3–7). Rubber catheters are most generally used. The ordinary Jaques' red rubber catheter is not now much employed in urological practice except as a splint. A Harris' catheter which is modified from the Jaques' has a hollow



Fig. 3. Olivary tipped—gum-elastic bougies

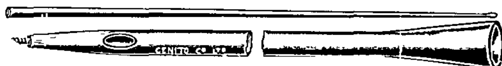


Fig 4. Phillip's catheter.



(*a*)



(*b*)



(*c*)



(*d*)

Fig 5 The common types of rubber catheter
(*a*) Jaques aseptic
(*b*) Harris
(*c*) McCarthy
(*d*) Tiemann

tip which will take a metal introducer and may therefore be made to pass when an ordinary rubber catheter cannot. A McCarthy resectoscope catheter is whistle tipped and is specially useful when small clots are forming in the bladder (Fig 5(*c*)) A Tiemann's catheter has an upturned or coudé end and is the most generally useful catheter for routine catheterization. It can be employed in the presence of enlargement of the prostate, and will also pass through a stricture. The Foley catheter is the best self-retaining

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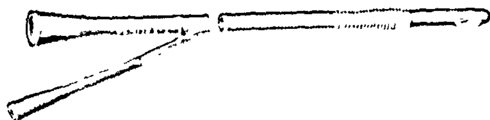


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urethral instrumentation There is no doubt however, that some form of local anæsthesia will help. This may be administered either in solution or in jelly, and is introduced along the urethra and kept in by employing a penile clamp.

Endoscopy. The large majority of instruments used in endoscopy for examination of the urethra and bladder employ a lamp at the tip and a telescope. One exception is the anterior urethroscope which may have indirect lighting.

Anterior urethroscopy: Indications:

(1) As a test for cure after urethritis.

(2) In chronic urethritis.

(3) In suspected stricture of the urethra.

(4) In repeated difficulty in instrumentation of a stricture when the presence of a false passage is suspected.

(5) In hæmorrhage from the penis, not associated with micturition.

(6) In suspected neoplasm of the urethra.

(7) In foreign bodies of the urethra.

The majority of pathological lesions seen in the anterior urethra are the result of urethritis, although exceptionally a papilloma soft infiltration, stricture, and less commonly leukoplakia may be seen.

Posterior urethroscopy: As a rule general anæsthesia is necessary. Indications:

(1) Hæmaturia occurring at the beginning or end of micturition.

(2) Bleeding from the urethra independent of micturition.

(3) In recurring papillomatosis of the bladder.

(4) In suspected bladder neck obstruction when a simple cystoscopy has not shown a cause.

(5) In chronic prostatitis.

(6) In prostatic calculus disease.

(7) In chronic posterior urethritis.

Cystoscopy. This is one of the most valuable and one of the commonest of urological investigations. An examining cystoscope consists of a sheath or hollow cannula which is angled at the tip. On this angle is fixed the lamp which provides illumination. At the other end there may be a valve, but preferably there are two taps to provide irrigation A telescope, which is a solid tube containing a series of prisms and mirrors with a viewing end outside and a window at the tip, can be passed along the sheath. The examining cystoscope has been modified to allow of manipulative procedure inside the bladder. The simplest modification is the instrument which carries an Albarran lever for catheterization of ureters. Catheterizing cystoscopes are usually angled but the McCarthy panendoscope is straight and through it rigid instruments may be passed and various operative procedures performed inside the bladder.

Indications for cystoscopy:

(1) Hæmaturia.

(2) Chronic infection including tuberculosis and Bilharzia.

(3) Suspected foreign bodies, such as stone.

(4) Frequency of micturition, without demonstrable cause.

(5) Enuresis in adolescents and adults.

(6) Bladder neck obstruction.

(7) Stone at the lower end of the ureter.

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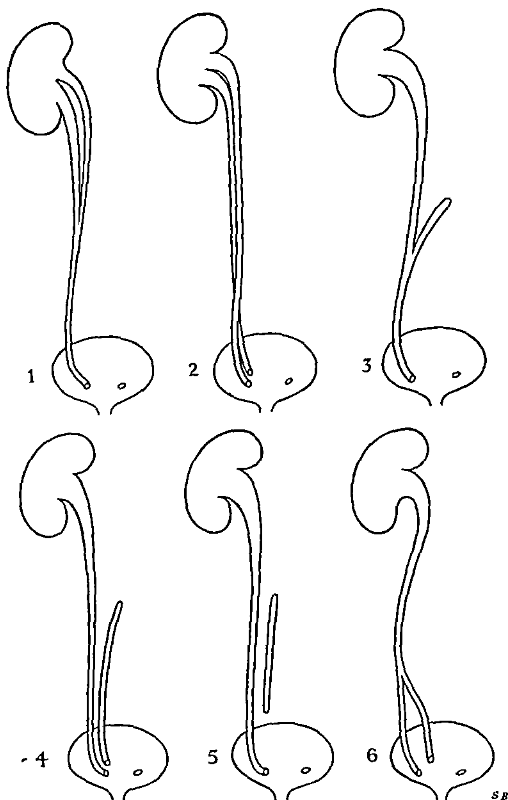


FIG 8 Diagrammatic representation of the possible abnormalities of ureters. (1) Incomplete, bifid at upper end (2) Complete bifid (3) Incomplete bifid but one end blind (4) Complete bifid but one end blind (5) Complete bifid but one part normal, the other blind both ends (6) Incomplete bifid at lower end (exceptionally rare)

KIDNEY AND URETER

Congenital Anomalies

Congenital abnormalities of the renal tract are of considerable clinical importance since they are frequently associated with diseases such as infection and calculus, and the latter conditions may be the cause of the patient's symptoms. It is convenient to consider the kidney and ureter together since both parts of the upper urinary tract are usually affected by an anomaly.

Renal Duplex or Double Kidney is the commonest congenital abnormality of the urinary tract. It more often affects only one side, but frequently both. There is duplication of the pelvis and the whole or part of the ureter. The ureter may be divided from the pelvis to the bladder, when there are two separate ducts, but more commonly the division is higher and the two ureters draining the pelves unite either one-third or half-way down and open as one into the bladder. The renal parenchyma is not completely separated into two although there may be lobulation and the blood supply is often separate with a definite vessel or vessels going to each half. If hemi-nephrectomy is necessary in such a case the separate blood supply makes the operation safer and easier to perform. Figure 8 shows the various types of division of the ureter which may occur. (1) Where it is incompletely divided, is the commonest. (2) There are two ureters. (3) There is a division but one ends blindly without any kidney tissue above it. (4) There is complete division with a blind end above. (5) and (6) are exceptional. Very rarely more than two divisions have been reported and instances have been found where there are as many as four separate ureters down to the bladder.

Fused or Horseshoe Kidney. The two kidneys may be fused together and the commonest way in which this occurs is by union between the lower poles. This condition is known as horseshoe kidney. Rarely, the upper poles are found joined together. Occasionally there is an asymmetrical fusion when the kidney is absent from one side and there is an irregular "L" shaped kidney mass on the other (*see* Fig. 9). In the commoner type of fusion the lower poles of the kidney may be joined by a complete thickness of renal tissue or the union may be mainly or entirely of connective tissue. The pelvis may be directed towards the mid line or it may point forwards or laterally. Some indication as to the position of the pelvis is obtained by the direction of the ureter as seen on urography. There is usually a multiple blood supply to each half of the fused kidney and the arteries vary in number up to ten, with three or four as the more common number. There is usually a direct supply to the isthmus. The inferior vena cava commonly lies behind the fusion but it may also be in front. Some degree of hydronephrosis is often found in a fused kidney. This predisposes to infection and to stone formation. In the horseshoe type of fusion some relief may be obtained by division of the isthmus and if this is composed mainly of fibrous tissue, the operation is comparatively free from danger. When the parenchyma as a whole is involved in the fusion, a good exposure is essential as bleeding may be profuse and the operation somewhat hazardous. When a stone has to be removed from the pelvis, the approach must be from the front and great care must be taken to identify the vessels. Exposure is more difficult since the lower pole of the kidney is fixed and cannot be delivered into the wound.

The Hypoplastic or Infantile Kidney. Occasionally, there is only a small cap of parenchyma, in which there may be little or no kidney tissue, attached to the ureter. In



(a)



(b)

FIG 10 (a) and (b). Ectopic kidney with stone in pelvis.

such a case, the kidney tissue is often thinned out and dilated, and the calyces are wide, short, and blunted. Usually the ureter is normal. It has been suggested that this hypoplasia is due to ischæmia which has occurred during fœtal life. The condition quite frequently gives rise to pain, the reason for which is difficult to explain. A hypoplastic kidney is often discovered accidentally in routine examination of the urinary tract and in such cases hypertension is occasionally present. The removal of a hypoplastic kidney has been followed by considerable or complete amelioration of the hypertension.

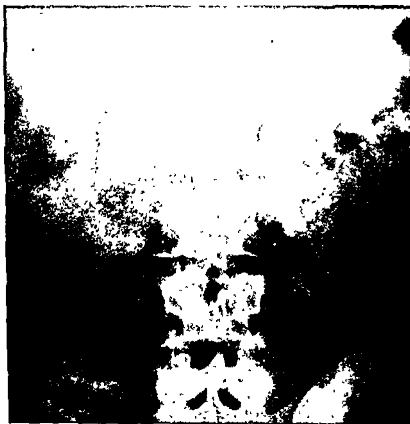


FIG 9 Fused kidney with left lying horizontally.

Unilateral Renal Agenisis. Absence of the kidney on one side has been found in 1 in 600 autopsies. As a rule the ureter is also absent; when present, it ends blindly at varying levels. If the ureter is completely absent, the inter-ureteric bar blends into the bladder wall about the middle of the trigone

The Ectopic Kidney. The kidney in its early stages of development is in relation to the upper sacral segments and the hilum points forwards By the fifth month, it has usually reached its ultimate position but on occasion may be found anywhere on the course from its early to its final situation An ectopic position must be differentiated from nephroptosis, and this is usually easily done if the length of the ureter is taken into consideration. A stone in an ectopic kidney may give rise to difficulty in diagnosis (*see* Fig. 10 (*a*), (*b*)). If the [illegible]

Errors in Rotation. I [illegible]

position, but this may f [illegible]


(a)


(b)

FIG. 10 (a) and (b). Ectopic kidney with stone in pelvis.

may give rise to difficulty in interpretation of the pyelogram in what appears to be a normally functioning kidney.

Abnormalities of the Renal Vessels. These are not infrequent and as a rule have not much clinical significance. Occasionally an abnormal vessel or an infra-polar vessel may play some part in either the production of a hydronephrosis or in the symptoms which arise from the hydronephrosis (*see* page 43). Branches from the renal artery are variable and not infrequently a polar artery arises quite early and more especially to the lower pole. Usually these are branches from an early division of the renal artery but they may arise as separate arteries from the aorta and occasionally have been found as branches of the internal, external, or common iliac artery, the hepatic, the middle sacral, the spermatic, inferior phrenic, and lumbar, pancreatic, or right colic arteries. Abnormal vessels are usually of no significance unless the kidney has to be exposed at open operation. If torn through they can give rise to troublesome bleeding and may even make nephrectomy necessary.

Abnormalities Affecting the Ureter only

Hydronephrosis and Hydro-ureter (*see* page 42).

Ectopic Opening of a Ureter. The ureter may open in an unusual place. An ectopic opening of the ureter is said to occur as frequently in the male as in the female, but in view of the rather different sphincteric arrangement in the two sexes it is rare for it to give rise to symptoms in the male, and therefore it is rare for it to be diagnosed. Kilbane has classified ectopia of the ureter in the following order of frequency:

	%
Complete unilateral duplication of pelvis and ureter with ectopic opening of one or other of the supernumerary ureters	52
[illegible]	31
[illegible]	11
[illegible]	3
[illegible]	1
Bilateral duplication of pelvis and ureters and bilateral ectopic openings	1

In nearly every case of ectopic ureteric orifice there is considerable interference with the function of the kidney and it is usually hydronephrotic. In the female, the opening may be in the urethra or in the vestibule of the vagina, and has been found elsewhere in the vagina, in the cervical canal and even in the fundus of the uterus. In the male, the ureter may open into a seminal vesicle, the vas deferens, or an ejaculatory duct, or into the prostatic urethra.

Symptoms. In the female, incontinence is the commonest presenting symptom and is paradoxical since the patient is often dry during the night and wet through the day. In the male, the condition is rarely diagnosed but may be suggested in chronic urinary infection with absence of a ureter on one side, or again if there is only one ureter with the suggestion of a renal duplex on one side and a cystic swelling is discovered in the region of a seminal vesicle or at the lower end of the vas

Treatment. When the ectopic ureter drains from a kidney which functions well it should be implanted into the bladder. This is not often the case. When the ectopic ureter drains part of a renal duplex, and this part of the kidney is hydronephrotic, heminephrectomy may be possible. Otherwise, if the contralateral kidney is normal, the ectopic ureter and kidney should be removed.

Stenosis. This may occur at the upper end of the ureter, usually at the pelvi-ureteric junction and give rise to hydronephrosis. When this occurs in childhood, a congenital origin may be fairly easily postulated, but in adults it is difficult to say that the stricture has not been acquired. The same applies to stenosis at the lower end of the ureter which is much rarer and may be a cause of mega-ureter (*see* page 51).

Ureterocele (*see* page 52).

Valves, Stricture, and Aberrant Vessels. A congenital valve or stricture of the ureter is rarely met with except at autopsy and then more especially in infants. An aberrant renal vessel may dip down and cause an obstruction in the upper third of the ureter. These conditions may produce regional dilatation of the ureter, i.e. the proximal part of the ureter. Treatment will depend on the degree of hydronephrosis above, and whether or not the other side is normal, and may take the form of plastic operation or a nephrectomy.

Diverticulum. Diverticulum of the ureter is very rare; and is usually discovered accidentally.

Congenital Dilatation of the Ureter or Mega-Ureter (*see* page 51).

Abnormalities in the Position of the Ureter. These occur in association with ectopia of the kidney or of the ureteric orifice. Otherwise, positional abnormalities are very rare.

Retro-caval ureter has been described in less than 50 cases and many of these were discovered at autopsy. The condition almost invariably occurs on the right side and is due to faulty development of the inferior vena cava.

Injuries of the Kidney

These may be closed or open.

Closed Injuries of the Kidney. In peace time most injuries are closed and are the result of traffic and industrial accidents, occur at games, or follow instrumental manipulations. Rarely, the spontaneous rupture of a diseased kidney has been reported. They are usually due to direct violence but may occur with acute forcible flexion of the spine in falling from a height. They occasionally occur after manipulations of the spine under general anæsthesia, and a catheter has been made to perforate the pelvis or parenchyma of the kidney during an instrumental pyelogram. A diseased kidney is of course, at least as liable to injury as a normal one when quite severe symptoms may follow a minor injury.

Pathology. That part adjacent to the hilum being the most fixed, is the most readily torn. A slight injury of the kidney may cause contusion without any tear of the capsule. In such a case there is always hæmaturia but this is often insignificant and clears up within 24 hours. In a severe case, the capsule is torn and there is extravasation outside the kidney together with an effusion into the pelvis of the kidney. Lacerations radiate regularly from the hilum and are thought to occur more often on the anterior surface and at the lower pole, since anatomically these parts are somewhat less protected. Rarely, the kidney may be torn in two, or a pole may be completely avulsed. The organ may be broken into several fragments or may be quite pulped. Exceptionally, it is split along the convex border and even more uncommonly may be avulsed from its pedicle Repair occurs by fibrosis. Broken tubules do not reorganize and there is atrophy of the glomeruli of the affected nephrons. In split injuries, where there has not been much destruction of the parenchyma, complete healing occurs, usually within 3 weeks. If on the other hand, there has been a severe contusion of the kidney, an extensive infarct occurs which will be replaced by fibrous tissue and may take weeks to consolidate. Wounds of the pelvis heal

by a linear scar If infection is severe there may be a brisk secondary hæmorrhage during the second or third week which may be so profuse as to necessitate urgent operation. An extravasation may take a long time to reabsorb. It may become infected and form an abscess or it may persist and become encysted causing the so-called pseudo-hydronephrosis.

Signs and Symptoms. There is a history of injury which has resulted in pain on the affected side; there may be swelling and there is nearly always hæmaturia. Immediately after the injury the patient feels nauseated and may faint, but recovery from both these symptoms usually occurs quite shortly. A dull ache remains in the loin and pain may become colicky if clots are being passed. Hæmaturia is an almost constant feature. The duration of bleeding will depend on the severity of the injury and whether or not infection has occurred. With slight injuries, there may be only a transitory hæmaturia and in more than half the cases, bleeding clears up in 7 days. In the more severe cases, it may continue for 12–14 days before ceasing If the injury is to a single kidney, oliguria or even anuria may occur.

The patient is usually a little pale and the skin moist and clammy. If bleeding has been severe, pallor will be marked, the pulse rate will be increased and the blood pressure will fall. The affected side is tender and the muscles are usually held tense. At this stage, a tumour cannot be felt in view of muscular rigidity. If the patient is conscious, the diagnosis can rarely be in doubt, but when there has been violence to a large part of the abdomen, it may be difficult to exclude injury to some other important viscus such as the liver or spleen.

In children, there is little or no perinephric fat before puberty. The peritoneum is in intimate relation to the kidney and if the latter is ruptured, then the peritoneum is frequently torn. Bleeding may occur into the peritoneal cavity and this may rapidly prove fatal

Complications. The important complications of renal injury are hæmorrhage and infection. Hæmorrhage may be immediate and urgent, or secondary and continuing. Infection may give rise to a perinephric abscess. In the large majority of cases, the kidney is the only organ damaged, but it may be one of many contused viscera. If the peritoneum has been torn and there has been an extravasation of blood, the bowel may become adherent to this site and acute intestinal obstruction may develop at a later date. Perinephric extravasation may not be absorbed in which case a large perinephric cyst will develop

Treatment of Injuries of the Kidney. If a diagnosis of a contusion of the kidney is made the patient must be put to bed. It is impossible in the early stages, to say what the progress of the case is going to be The pulse and blood pressure are taken frequently and it may be necessary to record these hourly, or even more often should the patient's general condition give rise to anxiety. Immediately after the injury, the patient as a rule feels a little sick and faint, and may lose consciousness and fall. Recovery is quite quick from this early stage of shock and the progress will, to a large extent, depend on the degree of injury and the amount of bleeding. The patient is kept completely at rest in bed, and is given morphia for pain. An estimation of the hæmoglobin concentration should be done and this is repeated should it be thought that he is bleeding. If shock is severe, the blood pressure is low, and an intravenous infusion of plasma or blood should be started. If he is able to swallow, fluids should be given by mouth. If there is no deterioration in the general condition, this conservative treatment should continue.

Hæmaturia by itself is not an indication for operation, nor is swelling in the loin, but if a swelling should be obviously increasing in size, or should the pulse rate go up and the blood pressure fall, with the patient under treatment, then operation must be undertaken as a life saving measure.

If, on the other hand, the patient's condition gradually improves an excretion urography should be done as soon as possible. The importance of this examination is to find out whether or not there is a kidney on the other side. In the early stages



Fig 11 Fourteen days after injury—still marked extravasation Retrograde pyelogram

after an injury to a kidney, even a small contusion may result in complete suppression of function, and there may be little or no excretion. Furthermore at this time, if the pelvis is full of blood clot there may be no delineation of it or of its calyces. Each specimen of urine voided should be examined and should be kept for comparison It is helpful if three consecutive specimens are available and preceding ones should be discarded in turn By examining these three specimens it is nearly always possible to see whether or not bleeding is subsiding In the large majority of cases, the bleeding clears up completely and the patient gradually settles down. In some cases however, where there is no urgent indication for operation bleeding continues and may persist for as long as 14 days before it ceases. If bleeding continues for longer than 14 days, a retrograde pyelogram should be done and if this shows gross extravasation nephrectomy should be advised (*see* Fig. 11) When it is decided to explore the kidney, the approach should always be through the loin. It is very unusual in a kidney injury that after exploration a conservative operation can be done It is much more common that the kidney requires

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In children, there is little or no perinephric fat before puberty The peritoneum is in intimate relation to the kidney and if the latter is ruptured, then the peritoneum is frequently torn. Bleeding may occur into the peritoneal cavity and this may rapidly prove fatal.

Complications. The important complications of renal injury are hæmorrhage and infection Hæmorrhage may be immediate and urgent, or secondary and continuing. Infection may give rise to a perinephric abscess In the large majority of cases, the kidney is the only organ damaged, but it may be one of many contused viscera. If the peritoneum has been torn and there has been an extravasation of blood, the bowel may become adherent to this site and acute intestinal obstruction may develop at a later date. Perinephric extravasation may not be absorbed in which case a large perinephric cyst will develop.

Treatment of Injuries of the Kidney If a diagnosis of a contusion of the kidney is made the patient must be put to bed It is impossible in the early stages, to say what the progress of the case is going to be. The pulse and blood pressure are taken frequently and it may be necessary to record these hourly, or even more often should the patient's general condition give rise to anxiety Immediately after the injury, the patient as a rule feels a little sick and faint, and may lose consciousness and fall Recovery is quite quick from this early stage of shock and the progress will, to a large extent, depend on the degree of injury and the amount of bleeding. The patient is kept completely at rest in bed, and is given morphia for pain An estimation of the hæmoglobin concentration should be done and this is repeated should it be thought that he is bleeding If shock is severe, the blood pressure is low, and an intravenous infusion of plasma or blood should be started. If he is able to swallow, fluids should be given by mouth. If there is no deterioration in the general condition, this conservative treatment should continue.

(*c*) A suture or ligature may occlude one ureter.
(*d*) Both ureters are occluded by suture or ligature.

(*a*) The Ureter is Divided and this is Observed at Operation. An attempt should be made to do a direct anastomosis of the ureter. When the division has occurred at the brim of the pelvis it should be quite possible to identify the two ends, to mobilize them and re-suture them. A rubber catheter of 8–10 Charrière size should be passed along the distal part of the ureter into the bladder with sufficient length for it to be brought out of the urethra. This latter event may happen fortuitously in the female and in about half the cases the tip of the catheter presents itself at the external meatus. Should however, this not happen and the catheter remains in the bladder, it must later be drawn out with cystoscopic forceps. When the division is low down, the upper cut end should be re-implanted into the bladder.

(*b*) The Ureter is Divided but this is not Noticed at Operation. The post-operative course is disturbed. The patient complains of lower abdominal discomfort and there is some pyrexia. On the affected side there is pain and tenderness in the loin and quite often there is pain in the iliac fossa The intake and output of fluids do not balance. In the most favourable case a uretero-vaginal fistula develops and the patient becomes incontinent. An intravenous pyelogram will show some dilatation of the ureter on the affected side. An attempt should be made to pass a catheter along the injured ureter. If this succeeds, the fistula may close spontaneously but if this does not happen the ureter is exposed extra-peritoneally and mobilized. In most cases it is possible to re-implant the upper end into the bladder. If this is impossible, a flap may be raised from the bladder wall and formed into a funnel (Boari's operation).

(*c*) A Suture or Ligature Occludes one Ureter A suture or ligature may occlude one ureter. This is not often recognized early Should it be suspected an intravenous pyelogram is done, a cystoscopy performed, and an attempt made at catheterizing the affected ureter. If the latter fails, the ureter should be exposed extra-peritoneally, and the obstruction removed. If a restoration of continuity has been possible, a careful follow up of the case is necessary as stricture of the ureter may occur.

(*d*) When Both Ureters are Tied. In this catastrophe the diagnosis is apparent early since there is a complete suppression of urine. An attempt is made at cystoscopy to catheterize the ureters. The orifices may not be seen on account of œdema of the trigone and in the region of the openings, but if seen and instrumentation fails, operation must be undertaken at the earliest possible time. The route chosen will depend on the previous operation. If this has been a pelvic floor repair, all sutures should be taken out and if the obstruction was due to simple kinking, urinary secretion will occur and the bladder will fill up. If this does not happen or the operation has been intra-abdominal then a mid-line incision should be made and one or other ureter is exposed extra-peritoneally. It is followed down towards the bladder and the obstructing cause having been reached, is then removed. If the patient's condition merits it, the other side should also be dealt with at the same time. On the whole, a nephrostomy is much less satisfactory although it may be necessary as a life saving measure.

Tumours of the Kidney

Benign tumours such as fibroma, adenoma, and supra-renal rests occur in the kidney and are seen at post-mortem examination. Occasionally, one may increase in size

to be removed. This obviously cannot be done if there is only one kidney and in such a case, should all attempts to stop bleeding by suture be ineffective, the contused area should be packed with one of the hæmostatic gauzes such as oxycel with vaseline gauze on top and the wound left open.

When the patient has completely recovered from contusion of the kidney without operation, and where the original pyelogram has failed to show function on one side, before the patient is discharged from hospital, a further intravenous pyelogram should always be done since the previous lack of function may have been due to some pathological condition in the kidney, which was there prior to the injury and perhaps predisposing to the hæmaturia resulting from the injury.

Open Injuries. These are very unusual in civil practice although not infrequent during war time. Bullet wounds usually destroy a portion of the parenchyma a little larger than the size of the missile. A piece of shrapnel, on the other hand, produces much more destruction. Stab wounds give rise to trouble only infrequently and then when the hilum is involved. When a kidney has been injured by a gunshot wound, there is usually an injury to one or more other important viscera and usually to part of the alimentary tract which may overshadow the renal injury. During war time, lack of equipment may prevent adequate investigation prior to operation. In such a case, it is essential that the opposite side should be explored in order to prove the presence of another kidney before an injured kidney is removed. Conservative operations such as partial nephrectomy or repair and plastic procedures are usually contraindicated in penetrating wounds because of the risk of infection. It is said that when urine escapes from a wound it is general that a nephrectomy has to be done. This is not by any means always the case. Since a greater appreciation of wound drainage and more scientific antiseptic treatment has been available, far more renal injuries have been treated conservatively with good results.

Injuries of the Ureter

Closed injuries of the ureter are very rare. It may be involved in a crush with fracture of a lumbar transverse process. Unless there is extravasation of urine or the development of an abscess the condition is likely to pass undiagnosed. A ureteric calculus, especially if irregular, may ulcerate through the wall of the ureter leading to extravasation. Gunshot wounds of the ureter are almost always complicated by injury to some other important viscus. This other injury is usually much more obvious since the alimentary tract is more often than not involved. The latter injury will be diagnosed and receive treatment at an early stage and at this time it is unlikely that the injury to the ureter will be noticed. Quite shortly extravasation will occur and the symptoms will then depend on the situation of the wound. A urinary fistula may appear or there may be a tender swelling in the loin. More often it is not until this has been treated and until urine appears in the wound that the diagnosis of ureteric injury is established.

Injuries of the Ureter occurring at Operation. Occasionally one, and sometimes both ureters are injured in the course of an operation in the bony pelvis. The surgical procedure has usually been extensive such as pan-hysterectomy or a resection of the lower part of the colon or rectum for malignant disease. The injury may be one of the following:

(*a*) The ureter is divided and this division is seen at operation
(*b*) The ureter is divided but this is not observed.

associated leukoplakia of the renal pelvis. The growth has a broad base with overhanging edges and ulceration of its central part. There is early spread through the pelvis to the perinephric fat and usually the growth is advanced when diagnosed. Metastases are common and early; and are found in the liver, lungs, brain, and other viscera and not infrequently in long bones.

Embryoma, Sarcoma, or Nephroblastoma. Wilms' name has stuck to this growth whilst that of Grawitz has been discarded in describing an adeno-carcinoma. This is the

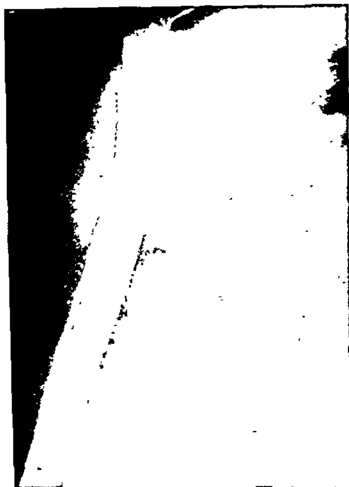


Fig 12 Secondary deposits in the head and shaft of the femur from adeno-carcinoma of the kidney.

only renal growth found in children. It nearly always occurs before the age of seven and is seen more especially from 1–3 years Very occasionally it has been found in adults and rather less than 40 cases have been reported in the literature. It is a solid growth occurring in the renal parenchyma and on section is bluish-white or grey in colour. Its blood supply is poor and necrosis with hæmorrhage readily occurs at the centre. It is not encapsulated and destroys the kidney by invasion. Histologically, the appearance is very variable but the section usually contains muscle and cartilage. It is a highly malignant tumour and has usually reached an advanced stage before it is diagnosed. The prognosis is very grave and very few children who have had this condition survive to adult life.

Symptoms and Signs. As in so many renal diseases, the classical symptoms are tumour, hæmaturia, and pain, and there may be a combination of these. A metastatic

sufficiently to give rise to symptoms A hamartoma is a rare benign tumour containing blood vessels, fat and muscle tissue. It is thought to be embryological in origin and may bleed spontaneously giving rise to severe pain. An angioma of the kidney may produce hæmaturia but it is rare for such a cause to be diagnosed except on histological examination of the kidney. It is exceptional therefore, for benign tumours to be of surgical importance. This does not include papilloma of the renal pelvis which in about 50 per cent of cases appears histologically to be benign. Tumours of the kidney which are of importance therefore, are:

Adeno-carcinoma or hypernephroma.
Papilloma of the renal pelvis.
Epidermoid or squamous-celled carcinoma of the renal pelvis.
Embryoma or nephroblastoma, often known as Wilms' tumour.

Adenoma-carcinoma or Hypernephroma. This is the commonest malignant tumour of the kidney and occurs anywhere in the renal parenchyma. It is at first encapsulated, solid and often golden yellow in colour. The latter is due to lipoid cells and especially to cholesterol. As the tumour grows, it becomes lobulated and cystic spaces appear in its centre. Bleeding occurs into the growth and often parts of it become pigmented and red. Rarely, areas of calcification are found either in the substance or in the circumference of the tumour.

Histologically, the tumour is composed of large, clear polyhedral cells with small deeply staining nuclei. These cells contain fat and are arranged in three fairly typical groups; glandular, papillary, and solid. In the glandular form, the cells are grouped as tubules or alveoli; in the papillary form there are branching processes, and in the solid form the cells are arranged in columns The course of an adeno-carcinoma varies tremendously and some indication of the prognosis may be given from the histological picture. Many are highly malignant, but in some cases a chronic course is pursued and the patient may live for many years without treatment. Whilst it is at first encapsulated, the growth spreads through the capsule directly to the calyces and pelvis of the kidney. It also spreads out into the perinephric fat and may invade the renal vein and grow along its wall or present into its lumen. Lymphatic spread occurs to the para-aortic glands and deposits may be found in the supra-clavicular glands Metastases also occur in the lungs, in bones especially the long ones, where the deposit is central, in the liver, in the skin and subcutaneous regions, in the erectile tissue of the penis, and rarely a secondary tumour has been found in the other kidney Sometimes, the metastasis may be the presenting symptom as in pathological fracture of a long bone.

Papilloma of the Renal Pelvis. This is a villous tumour resembling that found in the bladder and may be either single or multiple. It is composed of a series of fronds, each of which has a central core of connective tissue and vessels with branches resembling a conifer, the whole being covered by a layer of epithelium closely resembling that of the normal renal pelvis These transitional cell tumours have a tendency to form secondary growths in other parts of the urinary tract, the spread being in the direction of the stream Seedlings in the ureter are frequent and deposits may occasionally be seen near the orifice of the ureter on the affected side.

Epidermoid Carcinoma. This tumour also occurs in the pelvis and histologically may be either transitional-cell or squamous-cell At least half of these tumours are associated with stone and a still larger number with chronic infection of the kidney There may be an

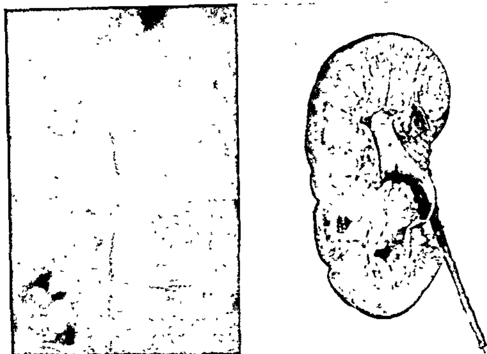


FIG. 14 Papillary carcinoma of the renal pelvis, invading the parenchyma. It has produced a filling defect in the pelvis on retrograde pyelogram. The two opacities on the outer side are gall stones.

(From the Annals of the Royal College of Surgeons)

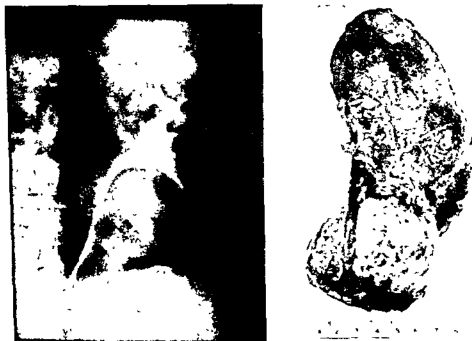


FIG 15 Adeno-carcinoma of the kidney with minimal distortion of lower calyx, and a soft tissue tumour of the lower pole showing on retrograde pyelogram

(From the Annals of the Royal College of Surgeons)

deposit may be the presenting symptom and rupture of the kidney has led to an acute abdominal emergency. Hæmaturia is usually the first thing of which the patient complains. It is usually painless although if profuse it may be accompanied by colic and may give rise to difficulty in micturition. It results when there has been spread to the calyces or the pelvis and occurs in a large proportion of adeno-carcinomata, in nearly all papillary and squamous-cell carcinomata of the renal pelvis, and in about half the



FIG. 13 Metastases in the lungs from epithelioma of the renal pelvis

cases of embryomata. The blood is always completely mixed with the urine and there may be clots, fine and worm-like when occurring in the ureter, and irregularly shaped when in the bladder. Bleeding may be so profuse that an acute retention of urine from clot occurs. It may follow exercise and often occurs after palpation of the tumour. If severe and long continued, it will give rise to exsanguination or to secondary anæmia. Less commonly, the tumour is the presenting symptom. An adeno-carcinoma when large may be discovered by the patient and quite commonly the embryoma is found by the mother on bathing the child In the later stages, it seems as if the emaciated shrunken infant is attached to the back of the tumour Pain may be due to colic from the passage of clots, or it may be a constant ache from involvement of the parietal wall by growth. Occasionally, the pain may be due to a pelvic growth producing obstruction and hydronephrosis and will occur in the exceptional case when extravasation from spontaneous rupture has

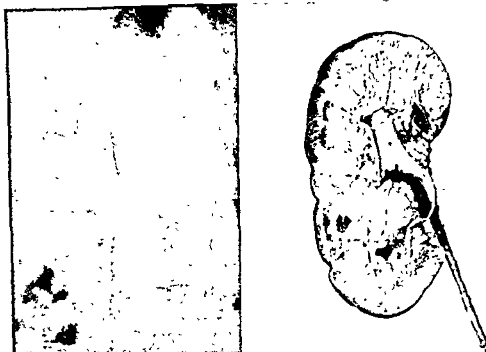


FIG. 14. Papillary carcinoma of the renal pelvis, invading the parenchyma. It has produced a filling defect in the pelvis on retrograde pyelogram. The two opacities on the outer side are gall stones

(From the Annals of the Royal College of Surgeons)

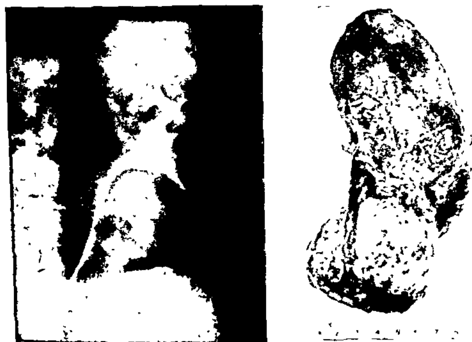


FIG 15 Adeno-carcinoma of the kidney with minimal distortion of lower calyx, and a soft tissue tumour of the lower pole showing on retrograde pyelogram

(From the Annals of the Royal College of Surgeons)



FIG 16. A torn off upper calyx from hypernephroma of the upper pole

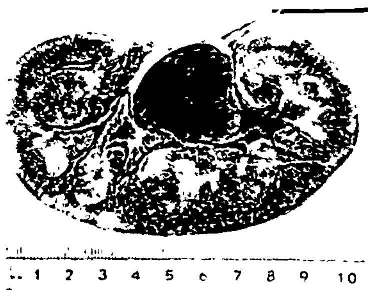




(a) (b)

FIG 17. Adeno-carcinoma (a) The pyelogram (b) The specimen showing destruction of the pelvis, lower and middle calyces and dilatation of the upper calyx by a hypernephroma showing much cystic degeneration.

(a)



(b)

Fig 18 Papilloma of the renal pelvis.
(a) The X-ray (Mr Harland Rees' case)
(b) The specimen

3



FIG 16 A torn off upper calyx from hypernephroma of the upper pole



(a)



(b)

FIG 17. Adeno-carcinoma (a) The pyelogram (b) The specimen showing destruction of the pelvis, lower and middle calyces and dilatation of the upper calyx by a hypernephroma showing much cystic degeneration

(a)



(b)

FIG 18 Papilloma of the renal pelvis.
(a) The X-ray (Mr. Harland Rees' case)

occurred. Caval block occurs when the growth has extended along the renal vein to reach and invade the inferior vena cava. There is a sudden painless œdema of both lower limbs and scrotum which as a rule is not fatal. If the co-lateral circulation is established the superficial veins of the upper and lower abdomen become markedly dilated and may be seen passing vertically like ladders up and down the abdominal wall. The œdema of the legs and scrotum then, to a large extent, subsides.

Metastatic Deposits. The commonest situation in which a metastatic deposit presents is in bone (*see* Fig. 12) and often with a pathological fracture. Quite often the diagnosis



FIG 19 Filling defect in pelvis with non-filling of the lower calyx shown on retrograde pyelogram The cut kidney shows an infiltrating growth of the pelvis which microscopically was a squamous-cell tumour.

(From the Annals of the Royal College of Surgeons)

of adeno-carcinoma of the kidney is only made when a biopsy of such a fracture has been obtained. Respiratory disorders have drawn attention to metastases in the chest (*see* Fig. 13) and secondary deposits have been found in the skin or subcutaneous tissues. Rarely an acute varicocele may make the patient seek advice. This occurs mainly on the left side and is not necessarily a bad prognostic sign.

Diagnosis. (*a*) *Adeno-carcinoma or Hypernephroma.* This is established by cystoscopy and radiology. Cystoscopy eliminates a bladder cause of hæmaturia and may demonstrate the side of origin of the bleeding. A bloody efflux may be induced by bimanual palpation of the kidney. An intravenous pyelogram may establish the diagnosis. It is suggested when deformity of a calyx is demonstrated or if it is cut off completely (*see* Fig. 17). There may be a filling defect of the pelvis (*see* Fig. 19), displacement of the pelvis and kidney either downwards or less commonly upwards, inwards, or outwards, depending on the position of the neoplasm. Occasionally, calcification is seen and this may be in the capsule when it will give a circular appearance, or there may be islands of irregular calcification. There may be no function shown in one kidney. In quite a large percentage of cases however, even when there is some function, the



FIG 20. A filling defect in the pelvis from a pure uric acid stone (Mr. Rupert Corbett's case).



FIG 21 A space filling lesion in lower half of the right kidney shown on intravenous pyelogram, proved on exploration to be a simple solitary cyst

(From the Annals of the Royal College of Surgeons)

delineation of the calyces and pelvis is not sufficiently good to reach an accurate diagnosis and a retrograde pyelogram must be performed.

(*b*) *Papilloma of the Renal Pelvis*. This may be suggested by finding a villus papilloma near the ureteric orifice in the bladder or when there is an area of diminished density or (*see* Fig 18) filling defect which is confined to the renal pelvis.

(*c*) *Epidermoid Carcinoma*. This is not often diagnosed before operation (*see* Fig. 19) and is usually discovered during or after a nephrectomy for a large stone in the renal pelvis.

(*d*) *Embryoma or Nephroblastoma.* In the advanced phase the diagnosis is usually obvious, since the tumour may not only be easily felt but may be seen. A sympathetico-blastoma is as a rule the only alternative and this tumour is more often found in older children and is usually more laterally placed than is the embryoma. If, on pyelogram, the delineation of the kidney is normal but is displaced downwards and inwards, it is suggestive of sympathetico-blastoma as is also so when there are areas of calcification.

Differential Diagnosis. (1) *A Non-opaque stone.* The outline of the filling defect is usually much more regular when due to a calculus than to a growth (*see* Fig. 20).

(2) *Cysts of the Kidney.* It may be impossible to differentiate a para-pelvic cyst from an early neoplasm of the kidney, radiologically (*see* Fig. 21). An aortogram may be helpful in such a case; there will be increased vascularity with "laking" when due to a neoplasm and diminished vascularity when due to cyst. When a lower polar cyst is large, and can be easily palpated, its consistency may be felt to be cystic rather than solid. It may be necessary to explore the kidney in order to arrive at the correct diagnosis. Adrenal tumours and other retro-peritoneal neoplasms such as a sympathetico-blastoma may all give rise to doubt but usually cause displacement of the kidney and pelvis without distortion or hæmaturia. Enlargement of the spleen may usually be differentiated by a blood cell count and examination, and a pancreatic cyst may be ruled out by bilateral pyelogram.

Treatment. Nephrectomy is the only effective treatment in the control of malignant disease of the kidney in the adult. It may be a considerable surgical undertaking and where the tumour is of any size, an intravenous drip transfusion should be commenced before the operation. If there is apparently only one secondary deposit in the bone and this can be excised with safety, it is justifiable to do a nephrectomy and to remove the metastasis by amputation. Should the metastasis have already been removed, nephrectomy should certainly be contemplated. Rarely, if a patient's condition is reasonably good, and repeated hæmorrhage from the kidney is causing severe disturbance, nephrectomy may be considered even if a metastasis is present. The operative procedure differs somewhat with the type of neoplasm. In adeno-carcinoma if the growth is large there is gross dilatation of the perinephric veins lying in the perinephric fat. For a growth of the lower pole, the best exposure is obtained with a transverse extension from the usual curved incision in the loin. This extension passes across the rectus abdominis muscle on the side of the lesion and if necessary opens the sheath of the rectus on the other side. Peritoneum is stripped off the front of the perinephric fat. The renal vein and inferior vena cava are felt for evidence of direct extension of the growth, and if they appear clear the pedicle is dissected free and the main vessels are divided between clamps taking care to clamp the artery first. Another exposure which has gained greatly in favour recently, is the trans-thoracic approach, between the tenth and eleventh ribs. In this approach the diaphragm is split and the kidney approached from above. It is especially indicated in lesions of the upper pole of the kidney.

Papilloma of the Renal Pelvis As spread of the growth occurs along the ureter any part of it may be affected, so the whole of it must be removed. It is essential to remove the intramural part of the ureter together with a cuff of bladder, since secondary carcinoma can occur in this situation and remain undiagnosed in a follow-up until too late.

Radiotherapy. There is some evidence that X-ray therapy may help after nephrectomy for adeno-carcinoma and epidermoid carcinoma. It is claimed that it may produce

amelioration in metastases. In embryoma, irradiation may be of great help. In certain cases where the tumour is very large, pre-operative treatment may change it from an inoperable to an operable case and such has also been reported in the case of adeno-carcinoma. It is not however, curative.

Tumours of the Ureter

Primary tumours of the ureter are not common; they may be simple papillomata, or malignant. Seedlings also arise in association with papillomatosis of the renal pelvis. The growth causes a gradual obstruction of the lumen of the ureter and usually gives rise to hydronephrosis leading to complete atrophy of the kidney. In the later stages the neoplasm invades the pelvic fascia and may then produce œdema of one or other of the lower limbs. There may be an elephantiasis of the scrotum and sciatica may be severe.

Signs and Symptoms. There are no typical signs or symptoms of tumour of the ureter. The condition may be suspected in a patient suffering from hæmaturia and aching pain, when there is no function on intravenous pyelogram and when an attempt to pass a ureteric catheter fails. A filling defect may be seen in a retrograde ureterogram.

Calculus Disease of the Kidney

The Formation of a Calculus. Some of the causes of formation of calculus in the urinary tract are quite apparent but many of these are not common and in most cases there is no clear-cut ascertainable cause for the occurrence of the stone. The causes may conveniently be discussed under three headings: (1) mechanical, (2) metabolic, and (3) miscellaneous.

(1) **Mechanical.** Any condition which results in stasis predisposes to stone formation. Most are congenital in origin but some may be inflammatory. Hydronephrosis—which may be limited to one calyx, when it is a hydro-calcycosis—and hydro-ureter are the chief abnormalities. Stasis may be induced by diminished diuresis and this is particularly seen in an individual who has transferred his habitation to a tropical climate and does not take sufficient fluid to flush out the kidneys

(2) **Metabolic.** (*a*) Dietetic Deficiency. The deficiency may be in Vitamin intake especially A and D and a low protein diet probably increases the excretion of insoluble calcium. A dietetic origin is believed to have been the principal cause of the high incidence of bladder calculus in this country up to the end of the nineteenth century. It was found especially in the labouring classes in the agricultural districts often in children, and more especially in those areas which were not pastoral. Primary vesical calculus is now very uncommon and this change is attributed to raising the standard of living and especially to the intake of an adequate supply of Vitamins A and D, to increasing the protein-carbohydrate ratio, and to a regular and adequate milk supply to children.

(*b*) Inborn Errors of Metabolism. Cystinuria, xanthinuria, and indigouria are all rare conditions especially the last. Cystine is found in about 3 per cent of cases of urinary calculi and such stones are usually pure; it is a familial disease and is transmitted by both the male and the female. Cases are not often observed before stones have formed, although crystals may be found in the urine without actual calculus formation. Precipitation occurs in an acid urine.

(*c*) Upset in the Uric Acid Metabolism. Uric acid is found in about 3 per cent of

cases and usually forms pure stones. Like cystine stones, they are usually bilateral and are always accompanied by a raised blood uric acid level. They are important clinically since they are non-opaque and may give rise to great difficulty in diagnosis.

(*d*) Upset in the Calcium-phosphorus Metabolism. Over 60 per cent of stones contain calcium and 40–50 per cent contain phosphates. The calcium-phosphorus metabolism is therefore of great importance. The normal serum calcium is between 9 and 11 mg. per 100 ml.; the normal serum phosphorus is between 2·7 and 3·7 mg. per 100 ml. In growing children and in adolescents this last figure may be 1 mg. higher. The products of the serum calcium and serum phosphorus figures is almost constant and is a useful level to remember. If the phosphorus or carbonate ions are lowered, the calcium ions will be raised and a hyper-calcuria will be produced. This condition is found in parathyroid disease, in acidosis, sometimes in Paget's disease of bone, and in Boeck's sarcoidosis.

(*e*) Hyper-parathyroidism According to Albright the parathyroid hormone makes the phosphorous ion in the body fluids more easily excreted by the kidney. With hyper-parathyroidism therefore, the serum phosphorus is lowered, the serum calcium becomes raised, and more calcium is excreted in the urine. This results in:

(1) Hypercalcuria and hypophosphaturia.
(2) Formation of stones in the kidney, or
(3) Nephrocalcinosis.

According to Albright nephrolithiasis or nephrocalcinosis occurs in 80 per cent of hyper-parathyroidism whilst bone changes occur in only 55 per cent.

(*f*) Citric Acid Metabolism. Citric acid metabolism may play some part in the prevention of stone formation. When there is an increased citrate excretion the calcium ion of the easily precipitated calcium phosphate may be replaced by the more soluble calcium citrate complex. Œstrogen increases the citrate content in the urine whilst androgen decreases it. In women, at certain phases of the catamenia there is an increase in the citrate excretion and this metabolic factor may play some part in the lower tendency for stone formation in the female.

(3) **Miscellaneous.** (*a*) Decubitus Stones These are found after prolonged immobilization particularly associated with injury or disease of the bone and are therefore, in part, due to reabsorption There is however, undoubtedly some effect from stasis since the incidence is diminished when steps are taken to overcome this by frequent change of position and adequate diuresis

(*b*) Infection Infection is present in about 30 per cent of cases of stone formation but whether this is cause or effect is not quite clear Dendritic calculus of the kidney is always accompanied by infection, usually staphylococcus albus or proteus vulgaris. This infection however, may not cause the stone formation but may determine its composition Soft phosphatic stones more often form in the bladder than in the kidney and are nearly always accompanied by infection, which is probably the cause of their formation.

(*c*) Colloidal Suspension Imbalance Normally urine is a supersaturated solution and this state is produced by a colloid suspension. Joly considered that interference with this colloidal suspension leads to a precipitation of crystals When an aggregation of these form, the nucleus of a stone is at hand and there is a continuing deposit or crystallization on this nucleus

(*d*) Sub-epithelial Plaque Formation. Randall suggested that sub-epithelial

plaques of calcium phosphate were of fairly frequent occurrence in the kidney especially in the tubules. He considered that these plaques ultimately extruded through the epithelium of the tubules to reach a minor or major calyx, or the pelvis, and they then formed the nucleus of a stone. This theory is supported by many observers but has not been properly substantiated, and Prien in a careful examination of the nuclei in a series of stones considered the evidence was against this as an origin.

(*e*) Foreign Body Nucleus. Apart from a collection of inspissated pus forming the nucleus of a calculus, it has been suggested that desquamated epithelium may also do so. Experimentally, if Vitamin A is excluded from the diet desquamation of the epithelium of the renal pelvis is produced and a calculus forms around the desquamated cells. Most athletes following strenuous exercise, are said to have transient hæmaturia. While the majority of the population are not athletes, it may be that any extra stress may in them, result in hæmaturia and that red cells may form the nucleus of a stone.

Apart from any demonstrable cause, such as an anatomical abnormality, or a known metabolic abnormality, Joly's colloidal theory would appear to be the most tenable.

The Composition of Calculi. A calculus may be formed of any of the substances which are found in the urine. It may be almost entirely of one salt or may be mixed. Twenty-five per cent of stones are formed of calcium oxalate, calcium oxalate and phosphate together account for another 35 per cent. Phosphatic calculi consisting of calcium phosphate and ammonium magnesium phosphate form 30 per cent. Urates and uric acid are 4–5 per cent; cystine 3 per cent; calcium carbonate, xanthin, indigo, and cholestrin account for most of the others. Rarely, a stone may form almost entirely of inspissated pus or of bacteria and a stone in the pelvis of the kidney or in the bladder, which has been there for a long time, may acquire a covering of muco-epithelial structure especially when a heavy infection is present. Calcium oxalate, cystine, and uric acid stones form in an acid urine and calcium phosphate and mixed phosphates in an alkaline urine. Calcium oxalate stones are usually very hard and irregularly shaped. This shape is due to crystallization; the urine is usually sterile and as has already been said, is acid. Phosphatic stones usually contain calcium phosphate, ammonium and magnesium phosphate, but there may also be some calcium oxalate or calcium carbonate present. When the urine is sterile, the stone is usually calcium phosphate, but when infected it is composed of triple phosphates The latter stone assumes the shape of the cavity in which it is formed and is the dendritic or stag-horn calculus of the kidney. It is rough, usually not particularly hard, and may be soft and crumbly. Calcium phosphate stones are hard, smooth, white, and when multiple are faceted. Uric acid and urate stones (4–5 per cent) are most commonly found in the bladder but do occur in the kidney. They are hard, often multiple, and rounded with a smooth or bosselated surface. These stones seem more prone to canalization and are non-opaque to X-rays. Cystine stones (3 per cent) are rather waxy, greenish in colour, occur in acid urine, and are found more frequently in the kidney than in the bladder They may be rounded, faceted, or dendritic. They are opaque to X-rays.

Calcium carbonate forming the whole of a calculus is rare (1–2 per cent). This is a very hard stone.

Xanthin, cholesterin, and indigo stones are very rare but have been described.

The Pathological Effect of Renal Calculi. The principal effect of stone on the kidney is due to obstruction together with the presence of infection. The degree of obstruction

will depend on the position of the stone and more often than not varies inversely with its size. A small stone impacted at the pelvi-ureteric junction may cause a hydronephrosis of considerable degree or may lead to complete suppression of function in that kidney. Conversely, the pelvis and calyces may be completely filled by a large stag-horn calculus; urine flows around it with little or no obstruction and there is only slight dilatation and, at any rate for a time, not much interference with renal function. A stone does not increase in size unless it is constantly bathed in normally concentrated urine. As has been said, a small stone impacted at the pelvi-ureteric junction causes a generalized hydronephrosis. On the other hand, the stone may remain in the calyx without causing any interference or may obstruct the neck, leading to local dilatation or hydro-calcycosis. When infection occurs in the presence of a stone, the picture usually is greatly altered. Pyelitis, pyelonephritis, or pyonephrosis may each occur. If the infection is limited to a simple pyelitis, this should completely subside after the stone has been removed, but should this be delayed, permanent thickening and fibrosis with rigidity of the pelvis occurs With infection and obstruction the parenchyma of the kidney atrophies, the calyces dilate, there is marked replacement of the kidney substance with fibro-lipomatous tissue, or multiple abscesses may occur throughout the organ and fibro-lipomatosis take place in the perinephric fat. Occasionally a perinephric abscess will form. In long standing cases of stone in the pelvis, especially if accompanied by infection, an epidermoid or squamous-cell carcinoma of the renal pelvis may occur.

Symptoms and Signs of Renal Calculi. These will depend to a large extent on the shape and size of the stone. If a small stone starts to move, especially if it is irregular, it will give rise to pain in nearly every case. Very rarely, a small stone has reached the ureter and has even been passed without any suggestion of renal colic, but this is very much the exception. Pain, when it occurs, is of two main types. Colic occurs with movement of the stone and usually means that an attempt is being made to pass it. It is not so characteristic of renal as of ureteric calculus There is a sudden, sharp, severe pain which begins in the costo-renal angle in the back. This pain passes through to the front and radiates downwards along the course of the ureter towards the scrotum in the male, and the labium majorum in the female. Less commonly, it radiates directly downwards to the thigh and very occasionally upwards towards the shoulder, when on the right side it may be mistaken for gall stone colic, and on the left for the pain associated with coronary disease. This colic will vary greatly in its duration and may last only a few moments or be more or less continuous for hours and in some cases a day or two In its severest phase the patient is writhing about and is unable to obtain any relief. He may sweat, be sick, and if the pain is very severe, may lose consciousness.

The second type of pain is aching in character and is usually associated with some degree of obstruction, either at the pelvi-ureteric junction or the ureter. If this obstruction occurs suddenly and is complete, then pain will be a predominating feature, and will gradually increase in severity until it reaches its maximum when it will remain stationary. In such a case, there will be general malaise and the temperature will be raised. With the onset of infection, pain also is a comparatively common feature. With a pyonephrosis there may be considerable pain in the affected loin together with a swinging temperature.

On examination of a patient suffering from colic, there is often not very much abnormal to make out in comparison with the severity of the symptoms; a little tenderness in the renal area with slight guarding of the abdominal muscles may be the only physical

findings. Occasionally, especially if there is a complete obstruction, an area of paræsthesia is found in the loin or high up in the iliac fossa. With an obstructed kidney in pyonephrosis, the kidney may be felt to be enlarged and tender. The tongue is furred and may be a little dry; the temperature is often raised and swinging. On examination of the urine, frank hæmaturia is seldom found but a centrifuged deposit will usually show some red cells, and if infection is present there will be organisms and pus. Occasionally, stone may cause frank hæmaturia, without any pain.

The large stones, especially the dendritic type of stag-horn calculus, present in an entirely different way. There is rarely pain, though occasionally a history of odd aches



FIG. 22 Massive dendritic calculi.

may be elicited after the stone has been demonstrated. Far more often however, the condition is discovered in the course of an investigation, which may be undertaken because of symptoms of dyspepsia and attention having been directed to the alimentary tract an X-ray is taken. A patient may present himself for an operation, or for entrance into a Service, or for life insurance and some abnormal finding in the urine, such as pus or albumen, makes investigation necessary. Many patients with large stones in both kidneys are surprisingly fit and can remain so for many years provided drainage remains free and infection remains minimal.

Diagnosis. It is rarely possible that the diagnosis of renal calculus can be made on physical examination. It may of course, be suggested by the history and if there has been a typical attack of colic and if the kidney region is tender, the assumption can be made that there is a stone either in the pelvis of the kidney or in the ureter. When a hydronephrosis has resulted from stone causing obstruction, then this may be felt. Very occasionally, in a thin patient multiple stones may be felt to produce crepitus, but the diagnosis really rests on X-ray investigation.

If a stone is suspected, an excretion urography should be done. The control film will show the presence of an opaque shadow (*see* Fig. 22). On lateral view if a shadow is in the kidney it will lie behind the level of the anterior surface of the vertebral bodies, but if there is a horseshoe kidney, the shadow will be a little anterior to this as will also be the case if a stone has entered the upper third of the ureter. In the upper abdomen an

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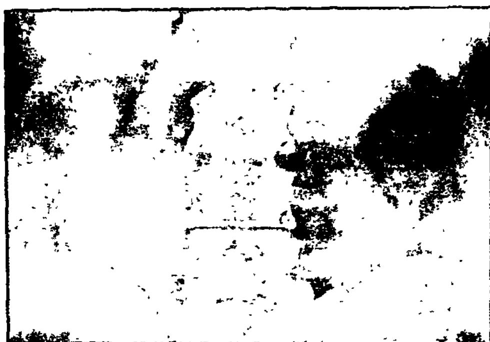
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opaque shadow may be caused by calcified glands, by phleboliths, and by calcification in vessels, especially if this occurs in an aneurysm of a renal or splenic artery. Other conditions which have at some time been mistaken for stone are calcification of costal cartilages, calcification in the parenchyma of a kidney from tubercle or neoplasm, or calcification in the wall of a cyst. The shape and density of the opacity may help.

Calcified glands have a fragmented appearance and an irregular edge. Phleboliths are homogeneous, circular or oval and with their margin smooth. Calcification in a vessel is usually somewhat tubular, although the signet ring appearance in an aneurysm is similar to that due to deposition of calcium phosphate on a non-opaque uric acid stone.

An excretion urography or a urogram may be most important in establishing the diagnosis (*see* Fig. 23) In doubtful cases pictures taken on inspiration and expiration show whether the opacity is constant in its relationship with the calyces or pelvis. It shows the kidney function and demonstrates the presence of a congenital or other abnormality in the kidney. It also shows the degree of obstruction, if any, in a calyx or in the kidney as a whole. A pyelogram is the only means of demonstrating a non-opaque calculus but care must be taken in a retrograde urogram that a filling defect has not been produced by an air-bubble. A similar sort of filling defect may be seen with a small neoplasm of the renal pelvis, but the outline of this defect is usually much more irregular than when due to a non-opaque stone, as a uric acid stone is usually circular or oval. The blood uric acid should be estimated and the type of crystal in the centrifuged deposit identified. Very occasionally, the exact cause of the filling defect may not be demonstrated until laparotomy and in such a case it may even be necessary to open the renal pelvis before deciding on the cause of a filling defect.

Treatment. If a patient is having pain the early treatment will be directed to its relief. When severe an analgesic, such as pethedine, or omnopon with atropin should be given. When the pain has settled and the patient is no longer in acute distress, investigation is undertaken with a view to confirming the diagnosis and demonstrating the exact position of the stone or stones, together with the delineation and function of the kidney. The treatment will then depend on whether the stone is likely to pass, whether it can pass but is unlikely to do so, or whether it cannot pass. If the stone is likely to pass then it should be left, the patient encouraged to drink large quantities of bland fluid, at least six pints per day, and also told to take exercise. A small stone with one axis of less than 0·5 cm. which is smooth and is not giving rise to severe symptoms or to obstruction may safely be left for a time, as in the majority of cases it will be passed spontaneously. If, on the other hand, the stone is irregular in shape or is causing dilatation above it, or is impacted at the pelvo-ureteric junction, it is unlikely to pass and should be removed by open operation. If a stone is large and of such a size that it is unlikely to pass, then it is potentially harmful, will almost certainly increase in size, will ultimately damage the kidney, and should therefore be removed. If a stone has produced a simple hydronephrosis of recent origin, this will completely subside after removal of the obstruction. If a pyonephrosis has resulted however, there will be some permanent dilatation especially of the calyces. If this dilatation is limited to one calyx, especially the lower, then not only should the stone be removed, but a partial nephrectomy should also be undertaken (*see* Fig. 24) When at all possible, the stone should be removed through an incision in the pelvis of the kidney. By this route, little permanent damage is done and the opening heals by a linear scar. On the other hand, if a stone is present in a calyx, especially if the pelvis



(a)



(b)

FIG 23.

(a) An opacity in the line of the left ureter opposite the lower border of the fourth lumbar vertebra

(b) Considerable dilatation and delay above the opacity indicating that it is in the ureter.

is of the intrarenal type, it may be impossible to reach it by this route and an incision must then be made through the kidney parenchyma and the stone removed by nephrolithotomy. If the kidney has been largely disorganized, and especially if infection has been present for a long time, the question of its removal will be considered. If the other kidney



FIG. 24 Multiple stones in the lower half of a single kidney, successfully treated by partial nephrectomy

is perfectly normal and has not been the site of stone formation, nephrectomy should be undertaken If on the other hand, a stone is present in the other kidney or there has been a history of stone having been present in the other kidney, the tendency should be to conservatism as far as is safely possible. In such a case, it may be advisable to drain the kidney for a period of some weeks after removal of the stone, and to attempt to clear up the infection completely by the use of suitable antibiotic treatment.

Bilateral Calculi. *Each type of metabolic stones such as those formed of uric acid,* of cystine, or due to para-thyroid disease is much more prone to be bilateral The treatment of these stones will depend to a considerable extent on the same considerations as were discussed in unilateral stone Several factors will help in deciding which side should receive priority. If on one side a stone has caused complete obstruction, and this kidney has ceased to function, it should be tackled first It may begin to excrete soon after removal of the stone but may not start until the other side has also been operated upon

when it has been stimulated by the temporary lowering of the function of its partner. If a stone on one side is causing partial obstruction and on the other side there is none, then the side of obstruction should be operated upon first. Similarly, if one stone is in the position potentially to cause obstruction, for example in the pelvis, and on the other side the stone is in a calyx, the pelvic stone should be removed first. A single stone is more likely to cause obstruction than are multiple stones. If there is little between the size of the stones, the position of the stones or in the degree of obstruction, then that side which shows the poorer function should be given priority since it may subsequently be stimulated by having its better partner temporarily upset.

Dissolution of a Stone. There is no known means of dissolving stones of the urinary tract by anything taken by mouth. Various attempts have been made to effect this and to prevent recurrence. Taking aspirin or aluminium gels, may be of help in some cases but claims for hyaluronidase and extract of madder root are probably quite unfounded. Alteration of the pH of the urine, acid for one week, and alkaline for the following has also been tried with little effect. These measures have been applied more especially in the prevention of the recurrent formation of stone in the urinary tract than in actual treatment. Local means have, however, been employed to attempt to dissolve stones with some measure of success and in this respect Suby's solution (Solution G) has been used. Some reduction in size of stone has been claimed when this solution has been dripped through a ureteric catheter passed retrogradely, but its application is not really practicable except through a nephrostomy. On the other hand, stones do, of course, pass spontaneously and portions of dendritic calculi have either broken or been washed off the main stone and been voided.

In the treatment of the large dendritic calculus however, Solution G may be helpful in the post-operative period, dripped through the kidney by way of a nephrostomy tube for the first 10–14 days, and it may help to remove any small particles of grit or sand that have remained after removal of the stone. The method is not entirely free from danger and great care must be taken in the preparation of the solution especially with regard to its pH. The method is not suitable in an attempt to dissolve a large dendritic stone which cannot otherwise be removed and should be used only as an adjunct to surgery.

The prevention of the recurrence of calculi may be helped by irradication of infection, and this should always be effected if possible; but diuresis by means of extra daily fluid intake is the simplest and most effective means of preventing further stone formation.

Stone in the Ureter

It is probable that all stones found in the ureter come from the kidney, with the possible exception of an occasional one which forms in a large mega-ureter. The majority of ureteric stones pass down to the bladder after one or more attacks of colic. Some however, are arrested, either because of their size or more often because of their irregular shape. There are three common positions in which a calculus is held up—(i) at the pelvi-ureteric junction, (ii) opposite the third or fourth lumbar vertebræ, and (iii) in the lower third of the ureter, especially near the bladder. If a stone is arrested in the ureter, several things may happen to it.

(1) It is passed in a further attack or attacks of colic.

(2) It is not passed and causes obstruction. There is then a dilatation of the ureter the stone and this dilatation spreads to the pelvis and calyces of the kidney.

is of the intrarenal type, it may be impossible to reach it by this route and an incision must then be made through *the kidney parenchyma and the stone removed by nephrolithotomy*. If the kidney has been largely disorganized, and especially if infection has been present for a long time, the question of its removal will be considered. If the other kidney



Fig 24 Multiple stones in the lower half of a single kidney, successfully treated by partial nephrectomy

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vague but there has usually been a sudden attack of pain on the affected side. On examination, there is tenderness with guarding and often true rigidity in the iliac fossa. It is unlikely that the correct diagnosis will be made before operation since on the right side appendicitis is simulated and on the left a rupture of a diverticulum in diverticulitis. At operation however, it may become apparent when œdema of the retro-peritoneal tissues is found and if not then considered, urine will escape from the wound within 24 hours.

The Diagnosis of Ureteric Calculus. As a rule the history is that of a colic and the diagnosis should not be overlooked. On the other hand there are many cases who appear to have suffered from urinary colic and in whom no stone is found on investigation. In the latter type of case a collection of crystals may have been passed and quite often an excess of crystals are found in the urine. If the history is not typical and examination is equivocal, then microscopic examination of the urine will show the presence of red blood cells in calculous disease. A white cell count will show leucocytosis in appendicitis or in diverticulitis.

An X-ray examination of the urinary tract will usually reveal the condition. It has been suggested that an intravenous pyelogram should be done in the early stages of an attack, but this is often difficult to arrange for administrative reasons. Furthermore, as a rule, there is a marked increase in bowel gas which masks any opacity and makes intravenous urography of little value. An X-ray examination should be made however, even if the stone is produced soon after the attack of colic. On the plain or survey film the renal area and the line of each ureter should be carefully examined for the presence of an opacity. Especially on the right side, calcified glands lying in the mesentery may prove difficult although usually their fragmented appearance, and the fact that they are more often multiple, help and in successive pictures they fail to keep a constant relationship to the skeleton. An excretion urography will usually prove that they lie outside the ureter. If a shadow lies exactly in the line of the ureter and is in it, then we should expect some dilatation (*see* Fig. 25). This does not always happen with a stone and may very occasionally occur when a gland has become attached to the ureter. If there is still doubt, a ureteric catheter should be passed. If it is not obstructed in the situation of the opacity, pictures should be taken with a shift, in order to demonstrate whether or not the opacity moves with the catheter and stereoscopic views may be helpful. In the pelvis, the most common opacities are phleboliths. These are usually multiple, rounded or oval, homogeneous and usually not directly in the line of the ureter. A small calculus may however, be present with multiple phleboliths. Uric acid calculi in the ureter give rise to considerable difficulty and are occasionally demonstrated with an excretion urography but may require the greater contrast of a retrograde examination. When suspected the blood uric acid should be estimated and will be found to be raised. A loop in the ureter seen end-on may simulate a calculus as may occasionally calcification in an artery. A dental fragment in an ovarian cyst has also been mistaken for a ureteric calculus. A stone in the lower end of the ureter gives rise to œdema of the bladder wall just above and in the region of the ureteric orifice and this is quite apparent on cystoscopic examination.

Treatment. If the diagnosis is quite certain the immediate treatment is the relief of the pain due to the colic. Pethidine, omnopon, and atropin or other analgesics are usually effective within a reasonably short time. Very occasionally however, they fail and in such a case more active intervention is necessary. A cystoscope is passed, a ureteric

(3) Urine flows freely round the stone and it increases in size and assumes the fat date-stone shape typically associated with a ureteric calculus. The increase is often rather concentrical and layer after layer is laid down. These may be seen on X-ray. The stone may increase longitudinally.

(4) Very rarely the stone may canalize—either completely or a rivulet run through one surface of it.

(5) There may be complete suppression of excretion of the kidney—a calculous anuria.

(6) The stone may ulcerate through the wall of the ureter and cause an acute emergency from extravasation

Symptoms and Signs. It is quite exceptional for a stone to be found in a ureter without causing pain, which is usually quite severe and quite sudden. It begins in the loin, passes through to the front, down into the iliac fossa, and from there it reaches the scrotum in the male and the vulva in the female. The patient is doubled up with the pain and writhes about in bed sweating and groaning. Nausea is usually present and there is often vomiting, which as a rule does not relieve the pain. The attitude of the patient is quite different in this colic from that in peritonitis such as from appendicitis or perforated peptic ulcer, when, despite the severity of the pain, the patient lies quite still. There is not usually any interference with micturition though occasionally as the stone reaches the lower end of the ureter and especially in the intra-mural portion there may be a little increased frequency. Occasionally, there is a little hæmaturia.

On examination, there is tenderness on the affected side. This tenderness is usually in the iliac fossa but may also be in the loin. On the right side, the pain is often confused with that of appendicitis and many patients who have had recurring attacks of ureteric colic, possess a scar from an appendicectomy. There is quite often muscle guarding but no true rigidity. Sometimes there is hyperæsthesia in the iliac fossa which indicates that the ureter is partially, if not completely, obstructed. Examination of urine may show a little macroscopic blood and there may be albumen present. A centrifuged deposit usually shows a few red cells and sometimes an excess of crystals.

Calculous Anuria. This results when both ureters or the ureter of the only functioning kidney becomes completely obstructed. It has been said that this can occur when only one ureter is blocked, the other kidney being quite normal This is a very rare condition and is then thought to be due to reflex action.

Pain may be slight and the patient gives a history of not having passed any urine for 24 hours or longer. Sometimes by the time he reaches hospital it may have been several days since any urine has been passed and there is then some general manifestation of a constitutional disturbance. The tongue is white, furred, and a little dry. The patient feels unwell, is constipated, and may complain of a headache. On the other hand there may be a clear cut history of a severe attack of colicky pain on one side and since that time suppression of urine. Without treatment the patient's condition deteriorates. The temperature is raised, the breath becomes ammoniacal, the tongue is glazed and is a white or dirty brown colour. In the later stages nausea and vomiting are quite common and although mentally the patient may remain amazingly alert, quite often there are convulsive fits, towards the end. The patient lapses into coma, often of short duration, and dies usually between the seventh and the tenth day.

Perforation of the Ureter. Very occasionally a stone may ulcerate through the ureter and give rise to extravasation in the retro-peritoneal space. The history may be a little

vague but there has usually been a sudden attack of pain on the affected side. On examination, there is tenderness with guarding and often true rigidity in the iliac fossa. It is unlikely that the correct diagnosis will be made before operation since on the right side appendicitis is simulated and on the left a rupture of a diverticulum in diverticulitis. At operation however, it may become apparent when œdema of the retro-peritoneal tissues is found and if not then considered, urine will escape from the wound within 24 hours.

The Diagnosis of Ureteric Calculus. As a rule the history is that of a colic and the diagnosis should not be overlooked. On the other hand there are many cases who appear to have suffered from urinary colic and in whom no stone is found on investigation. In the latter type of case a collection of crystals may have been passed and quite often an excess of crystals are found in the urine. If the history is not typical and examination is equivocal, then microscopic examination of the urine will show the presence of red blood cells in calculous disease. A white cell count will show leucocytosis in appendicitis or in diverticulitis.

An X-ray examination of the urinary tract will usually reveal the condition. It has been suggested that an intravenous pyelogram should be done in the early stages of an attack, but this is often difficult to arrange for administrative reasons. Furthermore, as a rule, there is a marked increase in bowel gas which masks any opacity and makes intravenous urography of little value. An X-ray examination should be made however, even if the stone is produced soon after the attack of colic. On the plain or survey film the renal area and the line of each ureter should be carefully examined for the presence of an opacity. Especially on the right side, calcified glands lying in the mesentery may prove difficult although usually their fragmented appearance, and the fact that they are more often multiple, help and in successive pictures they fail to keep a constant relationship to the skeleton. An excretion urography will usually prove that they lie outside the ureter. If a shadow lies exactly in the line of the ureter and is in it, then we should expect some dilatation (*see* Fig. 25). This does not always happen with a stone and may very occasionally occur when a gland has become attached to the ureter. If there is still doubt, a ureteric catheter should be passed. If it is not obstructed in the situation of the opacity, pictures should be taken with a shift, in order to demonstrate whether or not the opacity moves with the catheter and stereoscopic views may be helpful. In the pelvis, the most common opacities are phleboliths. These are usually multiple, rounded or oval, homogeneous and usually not directly in the line of the ureter. A small calculus may however, be present with multiple phleboliths. Uric acid calculi in the ureter give rise to considerable difficulty and are occasionally demonstrated with an excretion urography but may require the greater contrast of a retrograde examination. When suspected the blood uric acid should be estimated and will be found to be raised. A loop in the ureter seen end-on may simulate a calculus as may occasionally calcification in an artery. A dental fragment in an ovarian cyst has also been mistaken for a ureteric calculus. A stone in the lower end of the ureter gives rise to œdema of the bladder wall just above and in the region of the ureteric orifice and this is quite apparent on cystoscopic examination.

Treatment. If the diagnosis is quite certain the immediate treatment is the relief of the pain due to the colic. Pethidine, omnopon, and atropin or other analgesics are usually effective within a reasonably short time. Very occasionally however, they fail and in such a case more active intervention is necessary. A cystoscope is passed, a ureteric

(3) Urine flows freely round the stone and it increases in size and assumes the fat date-stone shape typically associated with a ureteric calculus. The increase is often rather concentrical and layer after layer is laid down. These may be seen on X-ray. The stone may increase longitudinally.

(4) Very rarely the stone may canalize—either completely or a rivulet run through one surface of it.

(5) There may be complete suppression of excretion of the kidney—a calculous anuria.

(6) The stone may ulcerate through the wall of the ureter and cause an acute emergency from extravasation.

Symptoms and Signs. It is quite exceptional for a stone to be found in a ureter without causing pain, which is usually quite severe and quite sudden. It begins in the loin, passes through to the front, down into the iliac fossa, and from there it reaches the scrotum in the male and the vulva in the female. The patient is doubled up with the pain and writhes about in bed sweating and groaning. Nausea is usually present and there is often vomiting, which as a rule does not relieve the pain. The attitude of the patient is quite different in this colic from that in peritonitis such as from appendicitis or perforated peptic ulcer, when, despite the severity of the pain, the patient lies quite still. There is not usually any interference with micturition though occasionally as the stone reaches the lower end of the ureter and especially in the intra-mural portion there may be a little increased frequency. Occasionally, there is a little hæmaturia.

On examination, there is tenderness on the affected side. This tenderness is usually in the iliac fossa but may also be in the loin. On the right side, the pain is often confused with that of appendicitis and many patients who have had recurring attacks of ureteric colic, possess a scar from an appendicectomy. There is quite often muscle guarding but no true rigidity. Sometimes there is hyperæsthesia in the iliac fossa which indicates that the ureter is partially, if not completely, obstructed. Examination of urine may show a little macroscopic blood and there may be albumen present. A centrifuged deposit usually shows a few red cells and sometimes an excess of crystals.

Calculous Anuria. This results when both ureters or the ureter of the only functioning kidney becomes completely obstructed. It has been said that this can occur when only one ureter is blocked, the other kidney being quite normal. This is a very rare condition and is then thought to be due to reflex action.

Pain may be slight and the patient gives a history of not having passed any urine for 24 hours or longer. Sometimes by the time he reaches hospital it may have been several days since any urine has been passed and there is then some general manifestation of a constitutional disturbance. The tongue is white, furred, and a little dry The patient feels unwell, is constipated, and may complain of a headache. On the other hand there may be a clear cut history of a severe attack of colicky pain on one side and since that time suppression of urine Without treatment the patient's condition deteriorates. The temperature is raised, the breath becomes ammoniacal, the tongue is glazed and is a white or dirty brown colour. In the later stages nausea and vomiting are quite common and although mentally the patient may remain amazingly alert, quite often there are convulsive fits, towards the end. The patient lapses into coma, often of short duration, and dies usually between the seventh and the tenth day.

Perforation of the Ureter. Very occasionally a stone may ulcerate through the ureter and give rise to extravasation in the retro-peritoneal space. The history may be a little

vague but there has usually been a sudden attack of pain on the affected side. On examination, there is tenderness with guarding and often true rigidity in the iliac fossa. It is unlikely that the correct diagnosis will be made before operation since on the right side appendicitis is simulated and on the left a rupture of a diverticulum in diverticulitis. At operation however, it may become apparent when œdema of the retro-peritoneal tissues is found and if not then considered, urine will escape from the wound within 24 hours.

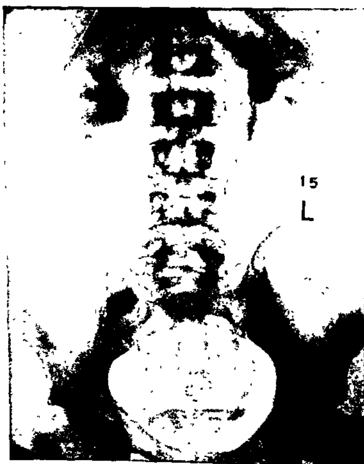
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(a)



(b)

FIG. 25 Stone in the lower end of the ureter showing dilatation
(a) Plain view.
(b) Intravenous pyelogram

catheter is introduced along the ureter and if it can be passed above the stone it is left in position. This will relieve the spasm and hence the colic. If, as is more usual, it cannot be passed above the stone, then 1 c.c. of local anæsthetic with or without a similar amount of liquid paraffin should be injected. More recently, for such a case, a ureteric catheter with a small balloon of the Foley type has been used and this of course will dilate the ureter, relieve the spasm, dislodge the stone, and may very well help in its immediate passage. If the stone is impacted and there is no colic present, an assessment must be made as to the necessity for interference. A smooth stone of a diameter less than 0·5 cm. in its narrowest axis can be safely left for a few weeks after the first attack of colic even in the presence of some dilatation of the upper urinary tract. A larger stone, or one which has produced dilatation for a longer period requires active intervention. In the upper third of the ureter, this must be by open operation. The ureter is exposed, an incision is made over the stone and it is removed. If the stone is more than 3 or 4 cm. above the bladder and removal is indicated, then again it should be done by open operation. If on the other hand, it is within 3 or 4 cm. of the ureteric orifice its passage may be helped by manipulation of a ureteric catheter passed endoscopically. If on cystoscopy there is œdema in the region of the orifice, then the stone is very near the bladder and possibly a simple incision with a Colling's knife or a tungsten wire electrode may allow the stone to present when it can be picked up and extracted with suitable forceps. If there is no change in the bladder wall around the ureteric orifice the stone is probably just above the intra-mural part of the ureter. Many ingenious instruments have been designed to assist its removal from the site. One of the most useful is the Ainsworth-Davis corkscrew and almost equally useful is the Johnson wire basket. This is a fixed basket and is safer than the Councill instrument which is expansible. None of these instruments is quite free from danger. On the other hand, there are many circumstances in which the acceleration of the passage of a stone at the lower end of the ureter may be of very great importance to the patient and in which this risk may be reasonably undertaken.

There are certain indications for surgical intervention in stone in the ureter, but not all of these are absolute and must be considered in conjunction with the symptoms of the patient. The indications are:

(1) When there is no excretion from the kidney on the affected side.
(2) When there is dilatation of the ureter above.
(3) When the stone is seen to be increasing in size.
(4) When repeated attacks of colic occur without progression of the stone.
(5) When there is suppression of urine—so-called calculous anuria.

SUBY'S SOLUTION (Solution G)

Citric acid monohydrate . . .	32·35	parts
Magnesium oxide anhydrous . .	3·84	
Sod. carbonate anhydrous . .	4 37	
Water	to 1,000	

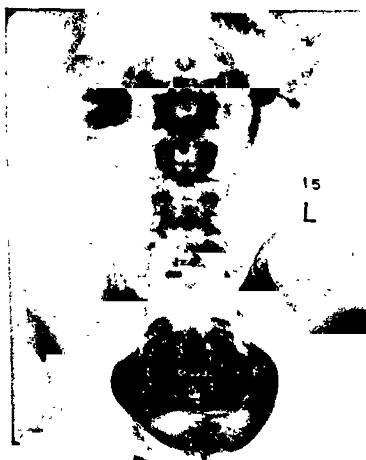
HYDRONEPHROSIS AND HYDRO-URETER

Hydronephrosis

The average capacity of the renal pelvis is about 7·5 ml. but the normal varies considerably above and below this. In hydronephrosis there is dilatation of the pelvis and/or



(*a*)



(*b*)

FIG. 25. Stone in the lower end of the ureter showing dilatation.
(*a*) Plain view
(*b*) Intravenous pyelogram.

catheter is introduced along the ureter and if it can be passed above the stone it is left in position. This will relieve the spasm and hence the colic. If, as is more usual, it cannot be passed above the stone, then 1 c.c. of local anæsthetic with or without a similar amount of liquid paraffin should be injected. More recently, for such a case, a ureteric catheter with a small balloon of the Foley type has been used and this of course will dilate the ureter, relieve the spasm, dislodge the stone, and may very well help in its immediate passage. If the stone is impacted and there is no colic present, an assessment must be made as to the necessity for interference. A smooth stone of a diameter less than 0·5 cm. in its narrowest axis can be safely left for a few weeks after the first attack of colic even in the presence of some dilatation of the upper urinary tract. A larger stone, or one which has produced dilatation for a longer period requires active intervention. In the upper third of the ureter, this must be by open operation. The ureter is exposed, an incision is made over the stone and it is removed. If the stone is more than 3 or 4 cm. above the bladder and removal is indicated, then again it should be done by open operation. If on the other hand, it is within 3 or 4 cm. of the ureteric orifice its passage may be helped by manipulation of a ureteric catheter passed endoscopically. If on cystoscopy there is œdema in the region of the orifice, then the stone is very near the bladder and possibly a simple incision with a Colling's knife or a tungsten wire electrode may allow the stone to present when it can be picked up and extracted with suitable forceps. If there is no change in the bladder wall around the ureteric orifice the stone is probably just above the intra-mural part of the ureter. Many ingenious instruments have been designed to assist its removal from the site. One of the most useful is the Ainsworth-Davis corkscrew and almost equally useful is the Johnson wire basket. This is a fixed basket and is safer than the Councill instrument which is expansible. None of these instruments is quite free from danger. On the other hand, there are many circumstances in which the acceleration of the passage of a stone at the lower end of the ureter may be of very great importance to the patient and in which this risk may be reasonably undertaken.

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Water	to 1,000	

Hydronephrosis and Hydro-ureter

Hydronephrosis

The average capacity of the renal pelvis is about 7·5 ml. but the normal varies considerably above and below this In hydronephrosis there is dilatation of the pelvis and/or

of the calyces of the kidney and most urologists would consider a renal pelvis with much over 15 ml. as constituting a hydronephrosis. The normal renal pelvis is subject to considerable variation in its relation with the parenchyma, but there are three main

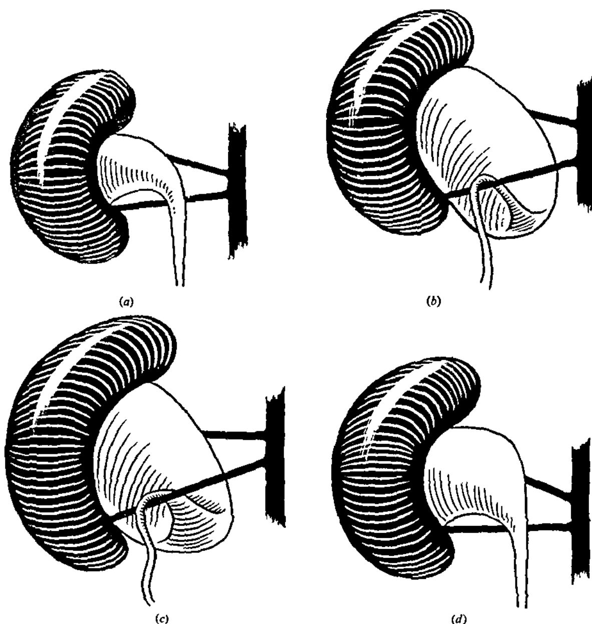


FIG 26 *Diagrams to illustrate the part played by aberrant or infra-polar vessels in hydronephrosis.*
(*a*) Normal pelvis
(*b*) A dilated pelvis

types: (i) The average type or extra-renal pelvis Here the pelvis is outside the parenchyma of the kidney, the calyces being surrounded by solid kidney tissue (ii) The intrarenal pelvis Here the pelvis as well as the calyces is largely surrounded by parenchyma. (iii) The third and least common type is when the greater part of the calyces as well as all the pelvis is outside the parenchyma The particular part to be most affected in

hydronephrosis will to some extent, depend on the type of kidney. Hydronephrosis may be confined to one kidney or it may affect both; it may be accompanied by dilatation of one or of both ureters.

Ætiology. It may be the result of a number of causes. Some are obvious, some are difficult to elucidate, and in some no cause is demonstrable. Many of the pathological conditions which commonly affect the kidney can obstruct the pelvi-ureteric junction, e.g. a small stone, a papilloma of the renal pelvis, or a stricture following inflammation.

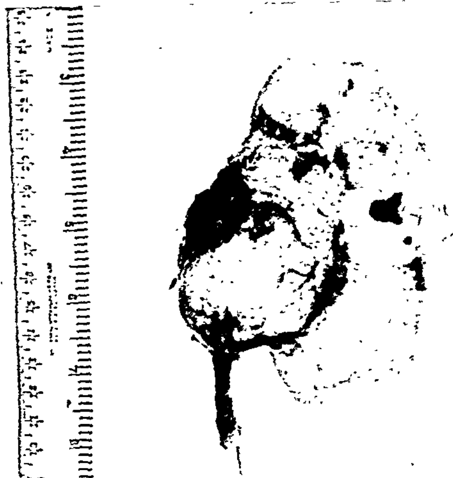


Fig. 27. A hydronephrosis with lower polar vessel. Note the upper part of the ureter is dilated.

Certain infections of the kidney cause the pelvis to become dilated and this is frequently an early sign in tuberculosis. The pelvi-ureteric junction may be obstructed from outside by fibrous bands, or by aberrant or infra-polar vessels. The upper end of the ureter may be kinked on itself by adhesions to the pelvis. The part played by aberrant or infra-polar vessels in the production of hydronephrosis has given rise to much discussion (*see* Fig. 27) One view considers that these vessels frequently cause hydronephrosis whilst the opposite denies that they can ever be the cause. It is probable that the correct answer lies between these two views and that aberrant vessels do cause hydronephrosis but do not do so very frequently Whilst these vessels may not cause hydronephrosis there is little doubt that they are often responsible for the presenting symptoms. Such vessels are quite frequently encountered at operation for hydronephrosis, and the dilated pelvis is then often found prolapsed between the two groups of vessels. This prolapse may produce a

complete obstruction, and in a few hours the kidney dilates up to the capacity allowed by the glomerular filtration pressure. This fairly sudden tension causes an aching pain which gradually grows in severity, reaches a maximum, and remains there until the obstruction is relieved or until the kidney gradually tires. On casual examination of such a kidney, the vessels may be thought to have occluded the ureter at the pelvi-ureteric junction. In the majority however, the obstruction from the vessel is not quite at the junction but is a short distance away from it, perhaps 1–2 cm. down the ureter. If the ureter between the pelvi-ureteric junction and the aberrant vessel is not dilated, the primary obstruction is at the pelvi-ureteric junction. In some cases however, the ureter is dilated right down to the obstructing vessel and then the aberrant vessel is the actual cause of the hydronephrosis (*see* Fig. 27) In most cases of hydronephrosis the cause of the condition cannot be clearly demonstrated until the kidney is exposed at operation; furthermore, it is only in a minority of these cases that the actual cause of the hydronephrosis is found and in the majority no mechanical abnormality is demonstrable. There is no evidence of obstruction either outside or inside the lumen or in the wall of the ureter or pelvis. The condition is then thought to be a neuro-muscular imbalance.

Pathology. The appearance of a hydronephrosis will vary with the type of kidney, with the cause, the degree, and the duration of the condition. In the commonest type of kidney the extra-renal pelvis is the part which is most obviously affected and the condition is then called a pelvic hydronephrosis. The parenchyma may appear to be fairly normal, whereas the pelvis is a widely dilated sac forming the greater part of the kidney mass. If on the other hand, the pelvis is intra-renal in type, it may be scarcely dilated at all and the affects of the obstruction are seen almost entirely on the calyces; the necks of the calyces become widely dilated and the normal cupping becomes flattened and later balloons out. The parenchyma becomes thinned out and atrophies so that in the severe degree it forms a shell to the many cavities large and small, of the calyces and pelvis. If a normal kidney is suddenly completely obstructed, the pelvis dilates slightly, the pressure quite quickly rises to some 50 ml. of mercury at which height filtration from the glomeruli ceases, secretion in the tubules stops, and there is anuria. The dilatation in such a case is negligible compared with that in the intermittently obstructed kidney. Here a large degree of dilatation may occur. A very large hydronephrosis is not very common nowadays, but cases have been reported where the kidney had contained over 30 litres of fluid. Following dilatation of the pelvis and calyces, the tubules dilate, the lining epithelium becomes flattened and atrophies, and the parenchyma is replaced by fibrous tissue. The intrinsic blood vessels are stretched, their lumen is narrowed and blood supply especially that carried in the efferent vessels, is diminished. As a result of this, increased atrophy occurs and the kidney shell is formed of fibrous inactive tissue.

Symptoms and Signs. There are few symptoms associated with an uncomplicated fully established hydronephrosis. Pain of some degree is usually present at some time and may be quite severe in the early stages, when the pelvis is beginning to dilate. Most children suffering from hydronephrosis present with severe attacks of pain in the loin. This may be almost colicky in character, is frequently accompanied by vomiting but it never radiates and there is no hæmaturia. This severe pain which is rarely met with in adults, occurs in the small hydronephrosis probably when the muscle of the pelvis is still capable of full contraction. An enormous hydronephrosis may remain quite symptomless unless some complication occurs and the swelling may then be discovered either

by the patient or by the physician. Symptoms of course, may be associated with the cause of the hydronephrosis, as for example the colic of a stone which has obstructed the pelvi-ureteric junction, the hæmaturia of a neoplasm or the frequency of tuberculosis.

When the hydronephrosis is intermittently obstructed, the history is usually fairly typical. At intervals, the patient experiences an aching pain on the affected side, gradually increasing in severity. At the same time a fullness is often noticed in the loin or in the epigastrium. This aching pain increases until it reaches a maximum at which it remains for some time, either hours or may be days. Then perhaps as the result of a change in position, perhaps by massaging the abdomen, or perhaps without apparent cause, the pain gradually diminishes. If a swelling has been present, then this also becomes less and concomitant with this is an increased frequency of micturition with polyuria. In the stage of obstruction there may be oliguria although this may not be noticed by the patient. Intermittent complete obstruction is always due to a mechanical cause and the most common of these is an aberrant vessel or a band at the pelvi-ureteric junction.

Infection in a hydronephrosis is not common unless instrumentation has been performed Should it occur there is pain on the affected side with an increase in temperature and often at the onset there may be rigors. Sometimes with infection, a hydronephrosis may become completely obstructed from œdema at the pelvi-ureteric junction and the same state may be produced by over-filling at a retrograde pyelography.

Stones, usually multiple, may form in a hydronephrosis and are probably the commonest cause of hæmaturia in this condition. As they are cushioned by the fluid in the pelvis or calyces pain is unusual. More often such stones are rounded and of varying sizes. Occasionally however, they may be faceted or a bizarre jackstone calcium oxalate calculus may form. It is very unusual for a stone, even a small one, to be passed spontaneously from a hydronephrotic kidney.

Rupture of a Hydronephrosis. The spontaneous rupture of a hydronephrotic kidney has been reported. More commonly however, such a kidney has ruptured following a comparatively trivial injury. The rupture then, is sometimes in the pelvis which is an unusual occurrence in a normal organ. Hæmaturia is not usually severe, and clears up within the first one or two days.

If the hydronephrosis is bilateral and severe, increasing renal inefficiency will ultimately give rise to symptoms of uræmia and this is likely to occur should the hydronephrosis become infected

The Diagnosis of Hydronephrosis. It is really only in the intermittently obstructed case with a fairly clear cut history that the diagnosis may be suggested. A smooth, cystic swelling may be felt in the loin on bimanual examination. It moves on respiration and is often ballotable. The degree of tenseness of this swelling will depend to some extent on the degree of obstruction It is not usually tender. If completely obstructed however, it becomes definitely tender and there may be guarding of the muscles overlying the kidney so that it cannot be accurately felt. Unless the kidney function has almost completely gone, intravenous urography usually establishes the diagnosis. If function has not been greatly disturbed, there may be a complete delineation of the pelvis and calyces. When quite severe, there may be only a few large opaque blobs which represent dilated calyces. Should there be no function at all, then the diagnosis may still be in

doubt until retrograde pyelography has been carried out. Usually, even with a large hydronephrosis, a catheter will pass into the pelvis or at any rate the dye will.

Less commonly, nothing passes into the kidney and the opaque medium runs down the ureter. As a rule this means a complete obstruction of the pelvo-ureteric junction



(a)



(b)

FIG 28

(a) A retrograde pyelogram with the ureter almost completely obstructed at its upper end.
(b) The specimen in this case showing a hydro-ureter with a lower polar vessel Note the upper end of the ureter is not dilated.

(*see* Fig. 28 (*a*), (*b*)) and sometimes a notch may be seen in this region which indicates that an outside band or aberrant vessel is the cause (*see* Fig. 29)

If a stone has produced the hydronephrosis, it can usually be seen on radiographic examination except when it is composed of pure uric acid. A filling defect in the pelvis of the kidney may then show on pyelogram, a similar appearance being given by a small neoplasm. When the hydronephrosis is due to tuberculous infection it is highly improbable that all the calyces will be completely regular and one at least usually shows a serrated edge indicative of ulceration. Investigation will show pus in the urine and usually acid fast bacilli will be demonstrated on bacteriological examination.

Bilateral hydronephrosis may be produced by the same conditions as cause the unilateral disease but there is usually no obvious cause when the condition then falls into the idiopathic group.

Treatment. An obvious cause such as a stone should be removed, but in the case of neoplasm or chronic infection such as tuberculosis, nephrectomy is the only practicable treatment. The large majority of cases however, do not present a certain cause until laparotomy and even then the ætiological factor may not be easily discernible.

In considering the idiopathic case therefore, several factors must be considered in assessing the best line of treatment. First of all whether or not operation is indicated by virtue of the symptoms or because of the progress of the disease. The results of conservative operations for unilateral hydronephrosis must be measured against the results



FIG 29 A retrograde pyelogram of a hydronephrosis suggesting pressure on the upper end of the ureter from without

of nephrectomy and nephrectomy therefore must be weighed against non-intervention. Many cases of hydronephrosis are discovered as the result of routine examination and do not in themselves give rise to much in the way of symptoms. More especially in bilateral disease, pain is the symptom which most often makes intervention necessary. Progression of dilatation over a period of observation and lowering of the total renal efficiency as evidenced by a rising blood urea or a poor urea clearance are other indications. In children, where the condition is nearly always accompanied by pain, operation is usually necessary if the condition is diagnosed. In adults however, the necessity for interference is usually consequent upon a complication, such as frequent attacks of intermittent

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Bilateral hydronephrosis may be produced by the same conditions as cause the unilateral disease but there is usually no obvious cause when the condition then falls into the idiopathic group.

and a little down the ureter. When sutured together, the pelvis capacity has been diminished to the extent of the excised segment and the ureter comes to drain at the most dependent part of this pelvis. If there is a high implantation of the ureter, instead of excising the flap it is better to turn it down from the anterior aspect, split the ureter for ⅔ cm. and suture this turned down flap to the edges of the two openings in the ureter thereby widening the upper end, after the manner of Ormond Culp (*see* Fig. 31(iii)).

If there is a very large pelvis, it must be dissected free and a considerable part removed, the ureter is cut across and is re-implanted into the most dependent part of the re-sutured pelvis after the manner described by Anderson and Hynes (*see Fig. 31(iv)*).

Some schools believe that minor degrees of idiopathic hydronephrosis are common and are a common cause of backache. Most of the larger series published include a very

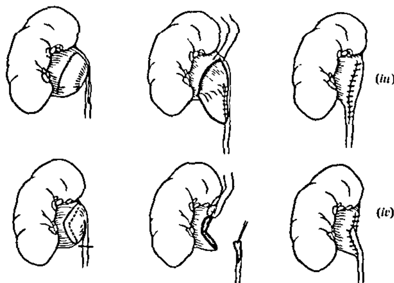


FIG. 31 Plastic operation for hydronephrosis
(iii) Culp (iv) Anderson-Hynes.

high percentage of women, backache in them is notoriously common, and there is some doubt that all these cases have in fact hydronephrosis. For idiopathic hydronephrosis renal denervation has been advocated. Stripping of the pelvis and hilum of the kidney after mobilization, is practised in some clinics and has been reported on favourably by Harris and Oldham The experience of other urologists is that whilst pain may be relieved, the kidney function is not always improved and indeed is sometimes worsened. If denervation is indicated, probably the better approach is by splanchnicectomy which is combined with removal of the first and second lumbar ganglia and division of the branches from the aortico-renal ganglion. More especially is this form of denervation of value in bilateral hydronephrosis and good results have been obtained when hypertension has also been a factor in the case

The operative treatment therefore, should be made to fit the individual case. It should be remembered that the only certain cure of hydronephrosis is nephrectomy and that whilst conservative operations should always be practised if operation is necessary on a bilateral hydronephrosis, when one kidney is normal and the other very dilated the most conservative operation may be nephrectomy.

complete obstruction, unrelieved complete obstruction, the appearance of infection in a hydronephrosis, or the presence of stones giving rise to recurrent attacks of hæmaturia. When it has been decided that some form of surgical intervention is necessary it is not always possible to plan the exact details until the kidney has been exposed and the hilum carefully inspected. It may be only then that the presence of bands, of aberrant vessels, of stricture in the pelvi-ureteric junction and even the presence of a small stone, may be first proved.

As has already been said in discussing the ætiology of hydronephrosis, aberrant or infra-polar vessels are frequently encountered in this condition. In many cases they are not the cause of the hydronephrosis, but are often an important factor in producing the symptoms which give rise to the necessity for operation. If the aberrant vessel is small

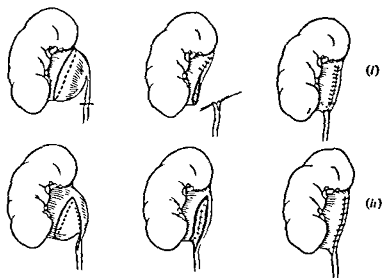


FIG 30. Plastic operation for hydronephrosis
(i) Lichtenberg. (ii) Foley

it may be clamped or temporarily occluded and the area of ischæmia of the kidney observed. If this is not great, the vessel can safely be divided between ligatures. If however, the artery is a big one division may produce an infarct of considerable size which can give rise to untoward effects necessitating nephrectomy. In such a case as this, especially if the kidney is an elongated organ, the plication operation introduced by Stewart which folds the kidney and hilum on itself, may be very suitable. This operation does not necessarily deal with the hydronephrosis but by approximating the two vessels it prevents prolapse of a dilated pelvis between them thereby preventing a complete obstruction Division of the vessel and removal of the ischæmic part of the kidney has been advocated. If there is narrowing of the pelvo-ureteric junction, this must be dealt with. If the dilatation of the pelvis is not very great, the simplest procedure is the Y–V plastic operation of Foley on the junction, thus widening the aperture Should however, the pelvis be considerably dilated some form of segmental removal appears to be necessary. The simplest type is a modified Lichtenberg resection (*see* Fig. 30) A wedge of the pelvis is removed from the inferior aspect, the lines of incision towards the body of the kidney are run to within 1 cm. of the junction between the inferior aspect of the pelvis and the parenchyma, whilst on the inner aspect they run through the pelvi-ureteric junction

orifice is quite normal but almost immediately above the bladder, the ureter dilates, often very widely even up to 3 or 4 cm. in diameter. This dilatation, in the less severe forms, may affect only the lower part of the ureter but in a large majority of cases it is dilated through its whole length. The pelvis of the kidney and calyces are also affected though to a much lesser degree and it is often a striking feature that the kidney is relatively normal, both in delineation and function, whilst the ureter may be an enormous tube.

(2) With obstruction at the ureteric orifice. The second type is where there is some



Fig 32. Mega-ureter—advanced state.

obstructive lesion at the lower end of the ureter. This may be a stricture, involving the whole of the wall of the ureter, at the orifice which prevents the admission of an instrument from below, or it may involve only the mucous and submucous layers of the orifice and give rise to a ureterocele. In the latter condition, each peristaltic wave distends the ballooned out lower end of the ureter, and there is then a constant trickle from the orifice until this ballooning deflates This repeats itself with each peristaltic wave along the ureter

(3) With a widely dilated orifice. The third and least common group, is where the orifice is widely dilated and is easily seen at cystoscopy. This usually means that even when the condition is unilateral it is due to some lower urinary obstruction.

Hydro-calycosis. This is the term applied to dilatation which is confined to a calyx or group of calyces. It is probably most commonly due to impaction of a stone at the neck of a calyx but may also occur if a stricture results from infection, or as the after effects of injury. A form of hydro-calycosis has been described where there is no obvious obstructive factor. It is then thought to be due to a neuromuscular imbalance at the neck of the calyx and may be congenital. Symptoms arising from hydro-calycosis are vague and atypical, and the condition can only be diagnosed after radiological investigation If a dilated calyx continues to drain into the pelvis it may not give rise to symptoms but should the neck become blocked and infection be present, there will be pain in the region of the affected kidney usually accompanied by fever, and sometimes by rigor. Drainage is usually re-established spontaneously quite quickly. The pain may last from 24–48 hours, when it suddenly subsides and gives place to frequency and burning on micturition often accompanied by slight hæmaturia. If the lesion is on the right side, it may simulate appendicitis during the first few hours.

Treatment. When the diagnosis is certain and the dilatation large, partial nephrectomy may be necessary. If on the other hand, it is small and due to a stone, removal of the stone may be followed by resolution of the dilatation. If the calyx is large and infected, and partial nephrectomy neither safe nor easy, then complete nephrectomy may be the best line of treatment.

Hydro-ureter or Mega-ureter

These terms are used to describe the condition when the whole or part of a ureter is grossly dilated. Dilatation may be confined to the lower part of the ureter when it usually arises at or near the intra-mural portion. The dilatation may commence higher up at the site of some obstructive focus whilst the distal part remains normal. The dilatation may affect the pelvis and calyces of the kidney as well as the ureter. It may be confined to one side or both ureters and kidneys may be affected, in which case the cause is nearly always obstruction of the lower urinary tract.

Segmental Dilatation of the Ureter. Rarely, this may be due to a congenital cause such as a stricture of the lumen, or an aberrant vessel or a band compressing the tube from the outside. It may be due to a neoplasm of the ureter then usually a carcinoma, but as this usually gives rise to complete lack of function on the affected side, the dilatation cannot be demonstrated prior to operation Rarely, it may be due to an adhesion outside the ureter, to a healed calcified tuberculous gland, to the stump of an appendix, or to the cæcum or abdominal wall following an appendicectomy. It may be due to a retro-caval position of the ureter. The commonest cause of segmental dilatation is a stone impacted in the lumen of the ureter. When this stone, as generally happens, is opaque to X-rays, it is easily demonstrated, but when the stone is a pure uric acid one, the diagnosis may be obscure. It may then be demonstrated by an intravenous pyelogram or a retrograde pyelogram, when a filling defect will be seen at the site of the obstruction.

Inflammatory strictures are uncommon in this country, and when they do occur are at the lower end of the ureter. They may be due to tuberculosis, or, in countries where the disease is endemic, to Bilharzia (*see* Fig. 32).

Dilatation of the Whole Ureter. (*See* Fig. 32.) This is nearly always congenital and three types are described:

(1) With a normal ureteric orifice. The first and commonest is where the ureteric

orifice is quite normal but almost immediately above the bladder, the ureter dilates, often very widely even up to 3 or 4 cm. in diameter. This dilatation, in the less severe forms, may affect only the lower part of the ureter but in a large majority of cases it is dilated through its whole length. The pelvis of the kidney and calyces are also affected though to a much lesser degree and it is often a striking feature that the kidney is relatively normal, both in delineation and function, whilst the ureter may be an enormous tube.

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In the second and third groups the obstructive cause can usually be demonstrated, but in the first group where the ureteric orifice is perfectly normal, and the passage of an instrument into the ureter is easy, the cause is mere conjecture. The condition is believed to be congenital, and its incidence is highest in children. It may affect both male and female children, but quite a number of cases do not appear to give rise to any symptoms until adolescence or even until the patient has attained adult life.

Signs and Symptoms. These may be dependent on the cause of the dilatation and in the majority of cases the condition will only be discovered on investigation, when some symptom such as pain, frequency, or hæmaturia has directed attention to the urinary tract. In the congenital forms of mega-ureter symptoms are unlikely until some complication supervenes. The most usual of these is infection and the next is stone formation. With infection there will be malaise, pyrexia, anorexia with frequency of micturition, and possibly rigors. It may settle down with treatment on several occasions. With stone formation there will be hæmaturia, but not often pain. With ureterocele the patient may complain of recurring attacks of aching pain. On the other hand the condition is quite often not recognized until a small stone is passed down the ureter. The ureterocele may be quite large however, and in itself may give rise to symptoms. The commonest of these is recurring ache in the iliac fossa, but it may produce acute retention by obstructing the internal meatus and occasionally in the female it has prolapsed through the internal meatus along the urethra to present in the vulva.

Treatment. The treatment of unilateral hydro-ureter will depend on the cause on the symptoms and on the function of the kidney above. If the dilatation is due to an impacted stone and infection is not a prominent feature of the case, the removal of the stone may lead to marked if not to complete recovery. If it is due to an outside occlusion of the ureter, the removal of this obstructing factor may have an equally beneficial result. Division of an aberrant vessel, or the freeing of adhesions with or without a plastic reconstruction of the dilated part of the ureter may leave the patient with a good functioning kidney. If the condition is due to neoplasm nephro-ureterectomy is always necessary. If due to a post-inflammatory stricture, an attempt should be made to dilate this, either from below, endoscopically, or if this is impossible, after exposure of the ureter. Should dilatation fail it may be possible to excise the stricture and reconstruct the ureter. If the kidney function is reasonably good, in a retro-caval ureter, the latter should be divided near the pelvi-ureteric junction, dissected free, brought round to the front of the inferior vena cava and reimplanted in the pelvis. A small ureterocele is treated by incision endoscopically using a Colling's knife or some other suitable ureteric meatatome. If there is a very large sac, part of it will have to be excised and this should be done transvesically through a suprapubic approach. If no cause is ascertainable, treatment will depend on the condition of the kidney and the presence of complications. If there is a good functioning kidney and infection is not present, or can be cleared up, it may be that operation is unnecessary Cases have been followed for a number of years after the accidental discovery of a large single hydro-ureter without the patient developing symptoms, or there being any deterioration in the function of the kidney. On the other hand, if attention has been drawn to the condition because of symptoms and especially because of infection, it is liable to recur and some form of surgical treatment will then have to be considered. Neurectomy has been suggested since the condition may be due to a neuromuscular imbalance and a division of the pre-sacral has been advocated as being the

simplest adequate approach. The results from this have been unsatisfactory and are likely to be so except perhaps in the very early case treated in infancy. Division of the ureter at its lower end with re-implantation into the bladder has met with some success, although there is considerable danger of severe infection spreading up to the kidney and an acute pyelonephritis ensuing, necessitating an urgent nephrectomy. Probably the most effective and satisfactory means of treating this condition conservatively is by a neo-ureterocystostomy in continuity. The lower end of the ureter is exposed, an incision is made longitudinally in the wall of the ureter as low as possible and an incision is made in the bladder adjacent to this. The two openings are then anastomosed. When the kidney above is functioning poorly, when stone formation is a common or significant feature, and when the other kidney is perfectly normal, nephro-ureterectomy is the most certain and safest treatment.

Bilateral Hydro-ureter. Rarely, bilateral mega-ureter may be due to the same cause as unilateral, but in the majority of cases there is an obstruction of the lower urinary tract, more especially at the outlet of the bladder. This obstruction may be from a muscle bar from fibrosis, from valves of the prostatic urethra or from congenital stricture elsewhere in the urethra. When the condition is found in children, adolescents, and young adults, the cause is often congenital. Occasionally, bilateral dilatation is due to enlargement of the prostate or to fibrosis of the prostate with or without calculus formation. It may occur in bladder growths when these involve the internal meatus or both ureteric orifices. The dilatation which occurs as the result of an acquired cause is nearly always of moderate degree whereas that associated with a congenital obstruction is often quite gross. When the cause is a lower urinary obstruction there is often but not always a reflux along the ureters on cystogram. It may be due to fibrosis in the pelvic fascia following irradiation of the pelvis either from X-rays or from cervical radium, and has occurred after extensive operations such as a Wertheim's radical hysterectomy or an abdominal or perineal excision of the rectum. Then the dilatation of each ureter begins about the brim of the pelvis.

A physiological dilatation of ureters, pelves, and calyces occurs during pregnancy. This begins in the early stages and is present until after parturition. A curious feature is that the right ureter and pelvis always dilate a little more than the left and no completely satisfactory explanation has been brought forward to explain this The dilatation occurring in pregnancy may be one of the factors accounting for the increased incidence of pyelitis and urinary infection during this physiological period.

Dilatation of the whole of both ureters may of course, occur with tuberculosis but it also occurs in a simple pyogenic infection such as with Bacillus coli. The dilatation as in all acquired cases is much less than is the congenital form and when the infection has been irradicated, the ureters will gradually return to normal size.

Cystic Disease of the Kidney

Simple Serous and Pyelogenic Cysts of the Kidney

This is a comparatively common condition in which one or more cysts are present in a kidney. If they remain small, they are discovered accidentally either at operation or at autopsy, but should one increase in size it may give rise to symptoms. Commonly the cyst is not very large but it may reach an enormous size and such a one has been reported as having almost filled the abdominal cavity. Those which give rise to symptoms are

In the second and third groups the obstructive cause can usually be demonstrated, but in the first group where the ureteric orifice is perfectly normal, and the passage of an instrument into the ureter is easy, the cause is mere conjecture. The condition is believed to be congenital, and its incidence is highest in children. It may affect both male and female children, but quite a number of cases do not appear to give rise to any symptoms until adolescence or even until the patient has attained adult life.

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Treatment. The treatment of unilateral hydro-ureter will depend on the cause on the symptoms and on the function of the kidney above. If the dilatation is due to an impacted stone and infection is not a prominent feature of the case, the removal of the stone may lead to marked if not to complete recovery. If it is due to an outside occlusion of the ureter, the removal of this obstructing factor may have an equally beneficial result. Division of an aberrant vessel, or the freeing of adhesions with or without a plastic reconstruction of the dilated part of the ureter may leave the patient with a good functioning kidney. If the condition is due to neoplasm nephro-ureterectomy is always necessary. If due to a post-inflammatory stricture, an attempt should be made to dilate this, either from below, endoscopically, or if this is impossible, after exposure of the ureter. Should dilatation fail it may be possible to excise the stricture and reconstruct the ureter. If the kidney function is reasonably good, in a retro-caval ureter, the latter should be divided near the pelvi-ureteric junction, dissected free, brought round to the front of the inferior vena cava and reimplanted in the pelvis. A small ureterocele is treated by incision endoscopically using a Colling's knife or some other suitable ureteric meatatome. If there is a very large sac, part of it will have to be excised and this should be done transvesically through a suprapubic approach. If no cause is ascertainable, treatment will depend on the condition of the kidney and the presence of complications If there is a good functioning kidney and infection is not present, or can be cleared up, it may be that operation is unnecessary. Cases have been followed for a number of years after the accidental discovery of a large single hydro-ureter without the patient developing symptoms, or there being any deterioration in the function of the kidney. On the other hand, if attention has been drawn to the condition because of symptoms and especially because of infection, it is liable to recur and some form of surgical treatment will then have to be considered. Neurectomy has been suggested since the condition may be due to a neuromuscular imbalance and a division of the pre-sacral has been advocated as being the

Treatment. The cyst should be removed with conservation of the kidney if this is possible. As a rule it is not possible to enucleate the cyst, and saucerization is all that is necessary. Occasionally, a partial nephrectomy is indicated and if the cyst is in one of the poles, this operation is quite feasible. Where the cyst is very large and has more or less replaced the kidney, the most practical procedure may be nephrectomy.

Congenital Polycystic Disease of the Kidney

This is a condition in which the parenchyma of the kidney has been almost entirely replaced by a large number of cysts. The condition is almost invariably bilateral although one kidney may be more affected than the other. There appear to be two types of the disease, that presenting in infancy and that in middle age. The condition in infancy known as the "infantile group" is congenital, may be a fœtal cause of difficulty in labour in the second stage, but more often presents either just after birth or during the first few months of life. The more common type is that which presents in middle age, namely "the adult group." This is familial, and it may be that the ætiology in the two groups is the same but Fergusson who has followed up numerous families has not found that the infantile and adult types are both recorded in the same family.

Pathology. The outline of the kidney is rather irregular and the cysts show through the capsule as blue knobs. On the whole, however, the organ roughly retains its normal shape. It is usually increased in size, the amount of increase depending on the number and size of the cysts. More often than not these cysts are more or less equal in size being anything from 1–3 cm. in diameter. The cysts seem to form more on the anterior than on the posterior surface of the kidney and in a well-marked case the organ appears to be entirely composed of these cysts, the parenchyma between them having undergone pressure atrophy and being replaced by fibrosis. In some cases, however, there are areas of practically normal renal tissue. The content of each cyst is usually clear but may be a little blood stained. It may contain uric acid, hippuric acid, albumen, creatinine, or other constituents of normal urine. There may also be red blood cells present with a little cholestrol. Microscopically the cyst is lined with epithelial cells, either cubical or flattened. Sometimes this epithelium proliferates and may show papillary buds projecting into the cavity. There is nearly always some degeneration of the glomeruli and tubules in the remaining renal parenchyma with varying degrees of dilatation of the tubules. It is rare to find that the cysts communicate either with a calyx or with the pelvis, but they do occasionally join with each other.

In the adult group somewhat similar cysts may be found in the liver, the spleen, and lungs, and exceptionally the thyroid and breast have been reported as being the site of cystic formation.

Symptoms and Signs. These may be (1) Uræmic, (2) Cardiovascular, and (3) Mechanical

(1) Uræmic. When there is renal insufficiency the patient becomes uræmic. This may occur gradually or suddenly; there is a general feeling of malaise, of lassitude, of lack of concentration with constipation, nausea, lack of appetite, an increase in thirst, and perhaps dimness of vision. The patient loses weight, and his general condition deteriorates. There is a change in the colour of the skin which at first is sallow but may later become quite bronzed.

(2) Cardio-Vascular Effects. The blood pressure is frequently raised and may be

usually at least as large as a cricket ball. The condition more often than not presents as a single swelling.

A simple serous cyst has a thin fibrous wall. The smaller ones may be para-pelvic but those which give rise to symptoms clinically usually project beyond the border of the kidney. Very rarely, a para-pelvic cyst may rupture into a calyx and give rise to one form of calycosis although it is of course really a diverticulum of the calyx. Microscopically, the wall is composed of fibrous tissue and is lined with flat tubular epithelium. The adjacent parenchyma of the kidney is atrophied from pressure. In the large majority of cases, the cyst wall is firmly adherent to the kidney and is extremely difficult to peel off. Occasionally, the wall may become calcified in part, although the cause of this is not known. Quite often, more than one cyst is present which would make it appear possible that this is an incomplete form of congenital polycystic disease. Another suggestion is that the cyst is due to an inflammatory tubular obstruction. Rarely, a cyst has been found to contain stones and it may then be a dilated minor calyx whose neck has become occluded. It is then fairly definitely a pyelogenic cyst.

Symptoms. These are not often severe. The patient complains of a dull, dragging ache in the loin or hypochondrium. If the cyst is large, it may be discovered by the patient himself or may be found on routine physical examination. It is very unusual for a cyst to give rise to symptoms on account of pressure on surrounding structures. Very occasionally, a small cyst may rupture into a calyx. This may be due to infection occurring in the cyst and at the time of rupture there may be pain, pyrexia, and a little hæmaturia. If the communication continues, a diverticulum has been established. There will be stagnation of urine which may become infected or stones may form. If the communication between the cyst and calyx is very narrow it may become blocked and will then give rise to intermittent attacks of pain together with temperature and tenderness in the loin building up to the point when the cyst ruptures into the calyx once more, when a similar clinical course to a pyelitis follows.

Diagnosis. The pre-operative diagnosis is usually made from the radiological appearance. In some cases, more especially in a para-pelvic cyst, it may be impossible to rule out a neoplasm on ordinary intravenous or retrograde pyelogram. In such a case an aortogram may be of considerable value. If a cyst is present the arteriogram will show a diminution in blood supply whereas if it is a neoplasm there will be a marked increase in the vascularity. If calcification is seen in the wall of the cyst it may be difficult to differentiate from a tuberculosis infection. A simple cyst is perfectly rounded and has a smooth wall. There is no irregularity such as is seen in the ulcerative type of tuberculosis. The remaining calyces, pelvis, and ureter will be quite normal apart from some compression if the cyst is in a position to produce it. In doubtful cases, it may be necessary to do a complete investigation in order to exclude a tuberculous infection. This will include a microscopic examination of the centrifuged deposit of repeated specimens of urine together with a culture of this urine and its inoculation into a guinea pig In a large infrapolar cyst the ureter may be displaced medially. One can diagnose the presence of a cyst with reasonable certainty when there is a rounded or spherical appearance of the space filling lesion, absence of hæmaturia or other abnormality in the urine, and complete normality of the remainder of the urinary tract, apart from some displacement of one or more of the calyces. There is no place for aspiration in the differentiation of the diagnosis.

Treatment. The cyst should be removed with conservation of the kidney if this is possible. As a rule it is not possible to enucleate the cyst, and saucerization is all that is necessary. Occasionally, a partial nephrectomy is indicated and if the cyst is in one of the poles, this operation is quite feasible. Where the cyst is very large and has more or less replaced the kidney, the most practical procedure may be nephrectomy.

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Pathology. The outline of the kidney is rather irregular and the cysts show through the capsule as blue knobs. On the whole, however, the organ roughly retains its normal shape. It is usually increased in size, the amount of increase depending on the number and size of the cysts. More often than not these cysts are more or less equal in size being anything from 1–3 cm. in diameter. The cysts seem to form more on the anterior than on the posterior surface of the kidney and in a well-marked case the organ appears to be entirely composed of these cysts, the parenchyma between them having undergone pressure atrophy and being replaced by fibrosis. In some cases, however, there are areas of practically normal renal tissue. The content of each cyst is usually clear but may be a little blood stained. It may contain uric acid, hippuric acid, albumen, creatinine, or other constituents of normal urine. There may also be red blood cells present with a little cholestrol. Microscopically the cyst is lined with epithelial cells, either cubical or flattened. Sometimes this epithelium proliferates and may show papillary buds projecting into the cavity. There is nearly always some degeneration of the glomeruli and tubules in the remaining renal parenchyma with varying degrees of dilatation of the tubules. It is rare to find that the cysts communicate either with a calyx or with the pelvis, but they do occasionally join with each other.

In the adult group somewhat similar cysts may be found in the liver, the spleen, and lungs, and exceptionally the thyroid and breast have been reported as being the site of cystic formation.

Symptoms and Signs. These may be (1) Uræmic, (2) Cardiovascular, and (3) Mechanical.

(1) Uræmic. When there is renal insufficiency the patient becomes uræmic. This may occur gradually or suddenly; there is a general feeling of malaise, of lassitude, of lack of concentration with constipation, nausea, lack of appetite, an increase in thirst, and perhaps dimness of vision. The patient loses weight, and his general condition deteriorates. There is a change in the colour of the skin which at first is sallow but may later become quite bronzed.

(2) Cardio-Vascular Effects. The blood pressure is frequently raised and may be

usually at least as large as a cricket ball. The condition more often than not presents as a single swelling.

A simple serous cyst has a thin fibrous wall. The smaller ones may be para-pelvic but those which give rise to symptoms clinically usually project beyond the border of the kidney. Very rarely, a para-pelvic cyst may rupture into a calyx and give rise to one form of calycosis although it is of course really a diverticulum of the calyx. Microscopically, the wall is composed of fibrous tissue and is lined with flat tubular epithelium. The adjacent parenchyma of the kidney is atrophied from pressure. In the large majority of cases, the cyst wall is firmly adherent to the kidney and is extremely difficult to peel off. Occasionally, the wall may become calcified in part, although the cause of this is not known. Quite often, more than one cyst is present which would make it appear possible that this is an incomplete form of congenital polycystic disease. Another suggestion is that the cyst is due to an inflammatory tubular obstruction. Rarely, a cyst has been found to contain stones and it may then be a dilated minor calyx whose neck has become occluded. It is then fairly definitely a pyelogenic cyst.

Symptoms. These are not often severe. The patient complains of a dull, dragging ache in the loin or hypochondrium. If the cyst is large, it may be discovered by the patient himself or may be found on routine physical examination. It is very unusual for a cyst to give rise to symptoms on account of pressure on surrounding structures. Very occasionally, a small cyst may rupture into a calyx. This may be due to infection occurring in the cyst and at the time of rupture there may be pain, pyrexia, and a little hæmaturia If the communication continues, a diverticulum has been established. There will be stagnation of urine which may become infected or stones may form. If the communication between the cyst and calyx is very narrow it may become blocked and will then give rise to intermittent attacks of pain together with temperature and tenderness in the loin building up to the point when the cyst ruptures into the calyx once more, when a similar clinical course to a pyelitis follows.

Diagnosis. The pre-operative diagnosis is usually made from the radiological appearance. In some cases, more especially in a para-pelvic cyst, it may be impossible to rule out a neoplasm on ordinary intravenous or retrograde pyelogram. In such a case an aortogram may be of considerable value. If a cyst is present the arteriogram will show a diminution in blood supply whereas if it is a neoplasm there will be a marked increase in the vascularity. If calcification is seen in the wall of the cyst it may be difficult to differentiate fr [illegible]

[illegible]

The remaining calyces, pelvis, and ureter will be quite normal apart from some compression if the cyst is in a position to produce it. In doubtful cases, it may be necessary to do a complete investigation in order to exclude a tuberculous infection. This will include a microscopic examination of the centrifuged deposit of repeated specimens of urine together with a culture of this urine and its inoculation into a guinea pig. In a large infrapolar cyst the ureter may be displaced medially. One can diagnose the presence of a cyst with reasonable certainty when there is a rounded or spherical appearance of the space filling lesion, absence of hæmaturia or other abnormality in the urine, and complete normality of the remainder of the urinary tract, apart from some displacement of one or more of the calyces. There is no place for aspiration in the differentiation of the diagnosis.

always present, and there are often casts on centrifuged deposit together with some red cells. As a general rule a culture is sterile. The blood urea may be raised. In a well-marked case, diagnosis can always be established by X-ray investigation, usually by intravenous pyelogram but when no function is seen certainly by retrograde examination. The calyces are elongated and often displaced, and there may be a long narrow communication between the major and the minor. This spidery appearance is fairly typical (Fig. 33). Occasionally the calyces are dilated rather like moose antlers (Fig. 34). The



Fig 34 Congenital polycystic disease

pelvis is frequently deformed and there may be a well-marked curve apparently produced by cysts indenting the calyx or pelvis. In certain cases even with quite a low blood urea, the concentration of dye is poor and insufficient to show the pelves or calyces. This does not necessarily mean that renal failure is imminent as the upset in function may be temporary and in six months time a good delineation of the pelves and the calyces may be obtained on urography.

Prognosis. When diagnosed at birth or in infancy, the expectation of life is short—less than a year or two. Of recent years, the condition appears to have been diagnosed more often in the early thirties than heretofore. This may be due to better methods of investigation including intravenous pyelography and more especially to urological investigation in cases of hypertension. Also, there is no doubt that more people continue to engage in regular pursuits in which minor traumata to the kidney may occur. Should there be hæmaturia an investigation will certainly follow and so the diagnosis may be established at an early age. In many instances there is a considerable time before the onset of renal insufficiency, and the patient may remain in a fair state of health for quite

the most important clinical sign or manifestation. As the result of this, headaches are quite frequent and there may be "black-outs" and attacks of dizziness. The patient may have an apoplectic convulsion followed by coma. This, indeed, may be a cerebral catastrophe due to a cerebral hæmorrhage following the hyperpiesis. On the other hand a somewhat similar clinical state may be a uræmic manifestation from complete renal failure.

(3) MECHANICAL EFFECTS. These are mainly those of tumour formation. In the infantile type tumour is the most usual presenting symptom and it may be the cause of

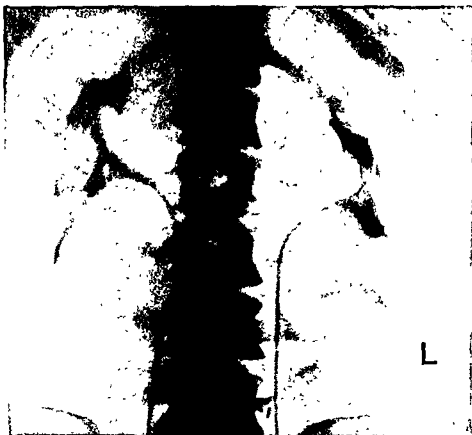


FIG. 33. Congenital polycystic disease.

obstruction in the second phase of labour. Tumour is much less likely to be the presenting symptom in the adult type although if attention is drawn to the abdomen then the swellings in each loin are easily felt on palpation. Symptoms may also arise as the result of the actual cyst formation. There may be recurring attacks of aching pain in the loin lasting for a few days and then after a variable amount of hæmaturia there is relief from the pain. It is probable that this syndrome is due to rupture of a cyst into a calyx, although this has not often been observed.

Diagnosis. As a rule the patient appears to be in indifferent health. He is usually pale, often thin, with sallow skin, and generally unhealthy appearance. On examination of the abdomen a tumour can be felt in one or both loins, usually more noticeable on one side than on the other. The tumour has much the same shape as the kidney but is irregularly knobbly and hard. It moves on respiration and is ballotable. The urine may be clear on examination or have a tinge of blood microscopically. Albumen is nearly

always present, and there are often casts on centrifuged deposit together with some red cells. As a general rule a culture is sterile. The blood urea may be raised. In a well-marked case, diagnosis can always be established by X-ray investigation, usually by intravenous pyelogram but when no function is seen certainly by retrograde examination. The calyces are elongated and often displaced, and there may be a long narrow communication between the major and the minor. This spidery appearance is fairly typical (Fig. 33). Occasionally the calyces are dilated rather like moose antlers (Fig. 34). The



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a number of years after a diagnosis of bilateral congenital polycystic kidney disease has been made. Undoubtedly however, the expectation of life is diminished and is shorter than in the average patient although a case has been known to live for 15 years after diagnosis.

When renal insufficiency is already present however, when the blood urea is raised and when the urine is solid with albumen it is unlikely that life will be greatly prolonged. In the last stages nausea, vomiting, obstinate constipation, and interference with vision are common symptoms and finally there is suppression of urine, albuminuric retinitis, and death (*see* p. 59).

Treatment. Nothing can be done to cure this condition and very little can be done to help it. The patient should be advised to lead a regular life without any over-indulgence and without strain. Rovsing's operation which consists of puncture of as many of the cysts as are accessible may have some place in the treatment, but this is doubtful. It may relieve pressure on kidney tissue and does allow of better functioning and more efficient drainage. This operation may be tried if pain is a significant factor in an individual case, although relief is probably temporary.

Cystic Formation in Pyelonephritis

Cysts may form in association with chronic pyelonephritis. They are then usually multiple and not very large. The ætiology is rather obscure but the condition is thought to be due to partial tubular obstruction. It is of little surgical importance but may be encountered when operating on a kidney.

Hydatid Disease of the Kidney

Hydatid disease is not common in this country although isolated cases do occur more especially in the sheep districts and in Wales and the Shetland Islands. It is occasionally found in Australia, New Zealand, and South Africa, also in Iceland and is quite common in the Middle East especially in the Balkans and in Turkey. The urinary tract is rarely affected, but the kidney and ureter have been involved and spread to the bladder has occurred when there has been pelvic disease. It may then be a cause of hydronephrosis either unilateral or bilateral.

Symptoms and Signs. These will depend on whether the infestation is open or closed. In the open type, daughter cysts or scolices are passed down from the pelvis of the kidney along the ureter to be voided in the urine. If they are discovered and identified, the diagnosis is of course, established In the closed form there may be tumour formation with calcification in the wall of the mother cyst, or of the daughter cysts or both. Casoni's intradermal test may confirm the diagnosis.

Treatment. If the condition is unilateral nephrectomy is usually the treatment of choice. Should this be contra-indicated, the cysts are exposed at operation, are devitalized by formalin, and then extirpated. To effect this a trocar is inserted into the cyst, half the contents are aspirated and then replaced by an equal quantity of 10 per cent formaline in saline.

Uræmia

Uræmia is the pathological state which develops as the result of considerable or total failure of kidney function Its onset is usually gradual over a period of many months.

but it may suddenly occur following some acute renal or extra-renal disaster. The kidney has certain important functions. The first of these is excretory. Most of the waste products of metabolism are excreted in the urine. Chemical and bacteriological poisons having been rendered harmless by the liver, are also excreted in the urine, as are certain foreign substances such as dyes and penicillin. The second important function is the regulation of the osmotic pressure of the blood. This is chiefly effected by the secretion or rather the control of salt excretion, especially chlorides. The third important function is the maintenance of the alkali reserve of the blood by the regulation of the hydrogen ion concentration. This is mainly affected by the manufacture of ammonia from amino acids and urea in the tubules, but also partly by the excretion of alkali and acid sodium phosphates salts. When renal function is upset, there is an interference with excretion. Waste products are retained in the blood and their concentration rises above normal. There is interference in the regulation of the osmotic pressure, there will be an alteration in the salt excretion especially chloride excretion; there may be retention of salt giving rise to hyperchloræmia and retention of fluid giving rise to œdema. The alkali reserve regulation may be upset and the CO_2 combining power drop far below normal. Amongst the biochemical changes, the most striking feature is the retention of urea in the blood. In uræmic conditions it is always raised above normal, but the degree of increase is not necessarily a true guide to the severity of a pathological lesion. A normal blood urea is 20–40 mg. per 100 ml.

In certain chronic uræmic conditions the patient can remain reasonably well with a blood urea level of 150–200 mg. for many months or even years. Occasionally, the blood urea remains below 100 mg. even when there is marked deterioration of renal function and the patient is undoubtedly suffering from renal failure. As a general rule however, this estimation gives a very good indication of total renal function. The urea retention is not necessarily the cause of the clinical syndrome known as uræmia. Probably the most important chemical upset is the interference with the acid base equilibrium. This control is most delicate, and an upset causes a marked change in general condition. In kidney disease, the mechanism loses its adequacy and ultimately fails. The CO_2 combining power diminishes, the alkali reserve goes down and acidæmia results. A co-existent anæmia makes matters worse as some of the buffering effect of hæmoglobin is lost. Besides this, the products of metabolism are retained, and abnormal metabolites accumulate.

Chronic Uræmia

This occurs in bilateral renal conditions such as chronic nephritis and pyelonephritis, congenital polycystic disease, bilateral lithiasis, and hydronephrosis. Increasing lower urinary obstruction such as is due to enlargement of the prostate, to a muscle bar or other bladder neck obstruction, and to stricture of the urethra will produce renal insufficiency Less commonly, it may occur as the result of bilateral stricture of the ureter following irradiation of the pelvis in a malignant disease and in some of the congenital causes of bilateral mega-ureter, urethra valves, and congenital bladder neck obstruction.

Symptoms and Signs. The onset of chronic uræmia is usually gradual and there may be a considerable degree of renal insufficiency before the patient is aware of anything being wrong. There is a general feeling of unwellness, with lassitude and inability to

concentrate on the daily business. There is usually some upset in the digestive processes with loss of appetite, nausea, occasional vomiting and constipation sometimes alternating with diarrhœa, and flatulent abdominal distension is not uncommon. As the condition progresses the patient becomes subject to headaches, is irritable, sleeps badly at night and yet feels drowsy through the day. In the later stages there is blurring of the vision from retinitis, sickness becomes quite common, polyuria and thirst increase, and in the final stages vomiting and convulsions occur.

On examination the patient looks unhealthy, has a sallow earthy complexion although occasionally the face is high coloured especially the nose. The tongue is rather dry and is furred, white or a dirty brown. In certain conditions producing chronic uræmia, the blood pressure tends to be raised, such as with bilateral pyelonephritis and congenital polycystic disease of the kidney. In the latter condition of course, both kidneys are nobbly and hard, and may be easily palpable. If a bilateral hydronephrosis is the cause of the uræmia, the enlarged, smooth cystic kidneys may be able to be distinguished clinically. If the cause of the uræmia is a lower urinary obstruction, the bladder may be felt to be over-distended rising high in the abdomen, often asymmetrically and not at all tender. The urine is pale with a low specific gravity often not much above 1,000. It contains albumen, with hyalin and granular casts, and quite often a few red cells will be seen on microscopic examination of a centrifuged deposit. In the later stages the polyuria which has been a marked feature will change to oliguria and towards the end there will be complete anuria.

Acute Uræmia

Acute renal failure may be due to several conditions and these may be conveniently discussed under extra-urinary, renal, and lower urinary causes. Amongst the extra-renal conditions which lead to acute renal failure is ischæmia following severe injury described by Bywaters and Beall as a "crush syndrome" and considered to be a lower nephron nephrosis. It may follow acute hypotension especially in a hypertensive and has been seen after extensive hæmorrhage such as occurs in gastric conditions, after an obstetrical emergency, or in extensive operations on the stomach. Amongst the renal causes are acute nephritis of toxic origin either due to infection or to chemical poisoning, to a tubular nephrosis following an incompatible blood transfusion, and to a similar sort of condition occurring with sulphonamide crystallization.

Amongst the lower urinary causes, the commonest is a calculous anuria. This of course, causes an acute uræmia and must be bilateral or occur on the only functioning side. Complete suppression has been reported when the other side is apparently normal. This is extremely rare and has been described as being reflex in origin.

Symptoms and Signs. These will of course, largely depend on the cause of the condition and the latter may very well mask the onset of the renal failure. Oliguria is usually the first abnormality to be noted and in the first few days after a severe injury, or in the immediate post-operative period after a genito-urinary or pelvic operation, or after a blood transfusion it may be noticed that very little or no urine at all has been passed In a day or two there is general malaise and headache of varying severity. The patient becomes irritable, resentful, restlessly drowsy, and sleeps badly. There is loss of appetite with nausea and quite often vomiting The bowels are constipated, there is marked increase in thirst, there may be itching of the skin, with tingling and numbness of the

extremities and cramp in the muscles. Hiccough is often a prominent feature and may be distressingly persistent. Quite often the patient remains very clear mentally, despite the occurrence of occasional convulsions. As the retained metabolites build up, muscular twitchings and cramps increase and there is exaggeration of the deep tendon reflexes. Headache may become very severe, there may be sudden blindness, local paralysis, monoplegia and hemiplegia may develop, and the condition terminates in convulsive coma and death. Without treatment, the length of period from complete suppresion to death is usually between 5 and 10 days.

Diagnosis. In the presence of a known renal disease or if a renal cause is demonstrable the diagnosis is not difficult. It may be difficult to differentiate a renal from an extra-renal cause, such as alkalæmia, (especially if the patient is taking alkalis in the presence of anæmia) cardiovascular disease, where the blood urea may be raised from renal congestion, and acidæmia from diabetes mellitus. A cerebral tumour and meningitis may also occasionally confuse the issue.

Treatment. If the cause can be removed, this should be done as soon as possible. When a stone is known to be blocking the ureter, it is removed and the kidney will quickly resume some, if not all of its function without much in the way of special treatment. In many cases however, treatment is not as clear cut nor as easy and certain facts and investigations are most important. An intake and output chart should be initiated on which all fluids entering or leaving the body must be included. The total intake is plotted against the total output for each 24 hours, and a balance made. The estimate of the blood levels of certain substances may be most important; such analysis may show an excess or a deficiency and as it is sometimes possible to correct these, this should be done as far as possible. The control of the electrolytic balance however, is extremely delicate, may be most difficult to achieve, and therapy can be fraught with danger.

The blood urea (normal 20–40 mg. per 100 ml.) is always raised. Regular and frequent tests give some indication both as to the progress of the case and to its prognosis.

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The alkali reserve (normal 55–65 vol. of CO_2 per cent) is quite often lowered and this may be so to a very considerable degree after ureteric-colic anastomosis. It seems to make the patient dyspnœic and nauseated.

The serum potassium may be raised but is more often lowered, which is thought to be an important factor in lassitude and weakness and may produce or aggravate ileus. A diminished serum calcium level produces much muscle irritability.

The intake and output of fluid must be balanced. After the relief of obstruction when this has been present in chronic uræmia, there is usually a marked polyuria so that diuresis is often the most important single factor in treatment, but with the polyuria, there may be electrolytic loss also If a patient has had an over-distended bladder and the prostate is removed, or the bladder is drained, it is essential that effective diuresis be kept up during the succeeding two or three days and that any electrolytic imbalance is corrected. Electrolytes and fluid should be replaced by mouth if possible. If insufficient can be given orally, the rectal route should also be employed and only when the alimentary tract cannot be made to absorb all that is required should other routes be employed The chief indications for using the intravenous route are:

concentrate on the daily business. There is usually some upset in the digestive processes with loss of appetite, nausea, occasional vomiting and constipation sometimes alternating with diarrhœa, and flatulent abdominal distension is not uncommon. As the condition progresses the patient becomes subject to headaches, is irritable, sleeps badly at night and yet feels drowsy through the day. In the later stages there is blurring of the vision from retinitis, sickness becomes quite common, polyuria and thirst increase, and in the final stages vomiting and convulsions occur.

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is not at all likely. Splanchnic block has also been suggested for the anuria of trauma, in cortical necrosis and others of the lower nephron nephrosis group. Here again, any improvement after such administration is likely to be a coincidence.

If anuria continues, attempt must be made to tide the patient over and to rest the kidneys as much as possible, in the hope that some spontaneous recovery of function will occur. The most hopeful practical method appears to be the regime advocated by Bull and his associates, who administer a peanut oil emulsion in drip through a nasal catheter. The solution contains:

Glucose . .	400 gm.
Peanut Oil	100 gm.
Acacia .	q.s.
Water . .	1,000 ml.

One litre is dripped in each 24 hours. If urinary excretion begins, an amount of water equal to that passed in the previous 24 hours, is added to the peanut drip. Any obvious upset of the electrolytic balance is remedied. All vomit is collected and returned to the drip. The peanut oil and glucose do not give rise to a nitrogenous residue but are sufficient to prevent excessive tissue breakdown. On such treatment a patient with anuria has been kept alive for as long as 30 days.

Dialysis is still largely experimental but in some cases has given hopeful results. There are three ways in which to apply this:

(1) Intestinal Dialysis.
(2) Peritoneal Dialysis.
(3) Blood Dialysis by means of an artificial kidney.

Intestinal Dialysis. For intestinal dialysis two Miller Abbot tubes are passed so that the end of one reaches the lower ileum and the end of the other is in the duodenum. Large quantities of iso- or hyper-tonic saline are run in through the upper tube and recovered through the lower Pyrah, for this purpose, has isolated a loop of ileum the two ends of which open on the abdominal wall.

Peritoneal Dialysis. For peritoneal dialysis a self-retaining rubber tube of the Malecôt or de Pezzer type is introduced into the peritoneal cavity in the epigastrium and a sump drain in the suprapubic region The dialysing fluid is run in through the epigastric tube and out through the other one. A modified Locke solution is used to which has been added penicillin, glucose, and heparin. Large quantities of fluid are required.

Artificial Kidney Dialysis. For blood dialysis some form of artificial kidney is employed. A number of these have been designed and used experimentally and to a very limited extent on clinical cases. In most of the models, the patient's blood is run off through cellophane tubing which passes through a bath of a prepared solution in which the blood is dialysed and is then restored to the patient. This method is of course, limited in its application to a centre which has the proper equipment and has not so far proved to be of much practical value.

Hypertension and Renal Disease

In certain conditions where both kidneys are affected, more especially in chronic nephritis and in congenital polycystic disease, hypertension is not uncommon and is often a prominent feature. Goldblatt (1937) showed experimentally that if the kidney on one side was rendered ischæmic a state of hypertension was produced. If subsequently

(1) When the substance cannot be retained in the stomach because of persistent vomiting or in the rectum because of insufficient absorption.

(2) When the substance to be given is likely to be altered or destroyed in the stomach or bowel.

(3) When a very rapid effect is required.

It should always be remembered that there are dangers in intravenous therapy. (1) The heart and circulation may be overloaded with too much fluid and pulmonary œdema will be produced. (2) There may be an allergic action, and (3) An infection may be introduced.

If there is oliguria the amount of fluid given must be carefully controlled and should be not more than 1 litre plus the amount of urine excreted in the previous 24 hours. Secondary anæmia is often a characteristic feature of chronic uræmia and if the hæmoglobin and red cells are lower than normal a blood transfusion should be given or intravenous iron administered.

If the blood chlorides are low, salt is given and if raised, salt intake is diminished or excluded. Acidæmia is counteracted by the administration of sodium bicarbonate or potassium bicarbonate together with potassium citrate. Alkalæmia may be counteracted by administering acid sodium phosphate. Regular action of the bowels is affected but strong aperients should not be given. If hypertension is a marked feature, venesection may sometimes help. On the other hand if there is marked hypotension this can often be corrected and a proper pressure maintained with an adrenalin or L-noradrenaline intravenous drip. Calculous anuria whenever possible, should be treated by removal of the stone rather than by draining above it. If oliguria occurs during the administration of sulphonamides, the latter are stopped and copious alkaline fluids administered. This usually affords relief, but should complete suppression follow ureteric catheterization is instituted and is nearly always followed by drainage and diuresis. It is considered by many that this is not an actual obstruction from the crystallization but is a tubular obstruction following desquamation of the tubular epithelium and is similar to ischæmic and blood transfusion anuria, and all of those conditions have been classed under one heading as a lower nephron nephrosis. There is no doubt however, that ureteric catheterization in the presence of sulphonamide anuria, may in itself be quite sufficient to overcome the crisis and drainage may be greatly helped by gently irrigating the kidney pelvis with a little alkaline solution such as a saturated solution of bicarbonate of soda. If the obstructing factor cannot be removed by such measures, a nephrostomy, pyelostomy, or ureterostomy must be performed above the level of the obstruction.

In most cases of acute suppression due to obstruction, as soon as the cause is removed, diuresis occurs, but should this not immediately happen, it may be advantageous to administer an intravenous solution of sodium sulphate—500 ml. of a 4·285 per cent solution is given and if excretion begins a further 1,500 ml. is administered during the next 12 hours.

After an incompatible blood transfusion 10 ml. of an isotonic solution of sodium lactate with 10 ml of a saturated solution of bicarbonate of soda have been given intravenously with some value. Occasionally, benefit has followed the intravenous administration of 4·285 per cent solution of sodium sulphate.

It has been suggested that early decapsulation of one or both kidneys will benefit uræmia from blood transfusion or toxic nephritis Most surgeons consider that this

cause. It is not uncommon in children especially in girls, and is usually confined to one side, but may be bilateral. It may be acute or chronic.

Acute Pyelitis. There may be a preliminary period of malaise or the attack may start quite suddenly with a rigor or even a succession of them. When the patient recovers from this he feels hot and feverish, and an aching pain is felt in one loin. During the next day frequency and a burning pain on micturition develop. Very occasionally there may be macroscopic blood in the urine. The patient is flushed, the temperature is raised often to 105 or 106°F., the tongue is furred, and the breath is offensive. There is tenderness in the loin on the affected side with some muscle guarding. A centrifuged deposit of the urine shows pus and organisms on culture. In the large majority of cases B. coli is grown.

Chronic Pyelitis. This may follow an attack of acute pyelitis, which has not completely cleared up. It is not uncommon in association with some other disorder of the urinary tract such as stone and with a congenital abnormality such as leads to stasis. The condition may remain sub-clinical and be a cause of chronic ill health with secondary anæmia, lassitude, and lack of mental concentration. Bilateral pyelonephritis may produce hypertension of varying degree. The infection may suddenly flare up and show itself intermittently as an acute illness.

Pyelitis Cystica. This is a rare condition which is nearly always associated with infection and is characterized by the formation of small cysts in the sub-mucous layer of the pelvis and usually also of the ureter. It is more often discovered accidentally on pathological examination of a removed organ but may be suggested by a "fluffiness" in the outline of the pelvis or ureter on X-ray.

Pyelonephritis

This is a more severe infection than pyelitis and involves the tubules and parenchyma as well as the pelvis. It is often an ascending infection associated with obstruction of the lower urinary tract and is characterized by the formation of multiple small abscesses in the renal parenchyma. Bilateral sub-capsular hæmatomata have been found in such cases on post-mortem examination. The infection may be acute or chronic.

Acute Pyelonephritis. This is almost always an ascending infection and is especially associated with prostatic obstruction but may occur after transplantation of a ureter and especially when such a ureter has been obstructed. There is a rise of temperature, often swinging, the tongue is furred, the bowels constipated, and the output of urine is diminished. There is sometimes pain in the loin but this is not common. When bilateral, and this is especially associated with lower urinary obstruction, the disease pursues a fairly rapid course. If untreated, oliguria is followed by anuria and the patient dies in uræmia.

Chronic Pyelonephritis. This is often rather a silent disease in which the infection of the kidney may gradually clear up and be followed by fibrosis of the parenchyma. In such a case multiple small cysts often form in the substance of the kidney. The symptoms are similar to those of chronic pyelitis but more often there is some degree of hypertension. As the condition is nearly always bilateral, it is not amenable to surgical treatment.

Carbuncle of the Kidney

This is a localized pyelonephritis limited to one part of the parenchyma. The infection is always hæmatogenous and results in the formation of single or multiple abscesses which coalesce. The infecting organism is almost always staphylococcus aureus. The

this kidney was removed the blood pressure suddenly and quickly returned to normal. This experimental finding provoked tremendous interest, and for a period, exhaustive urological studies of cases of hypertension were made from the renal pathology viewpoint. As a result of these studies, it was at first thought that unilateral kidney disease might be responsible for the hypertension in a considerable number of cases, and many nephrectomies were performed in the hope that operation would be followed by a permanent lowering of the blood pressure. A follow up of these cases, however, showed that the hypertension frequently recurred and that probably the worse of two affected kidneys had been removed. Nevertheless, there is no doubt that occasionally a clear cut case of unilateral renal disease does produce malignant hypertension and the latter is relieved when the kidney is removed. The cases which give the most favourable results are those in which there is evidence of interference with the blood supply to one kidney, e.g. where there is a renal aneurysm, where there has been some obstructive injury and in congenital hypoplasia of the kidney which is thought to be due to a congenital ischæmia. When nephrectomy does cure or ameliorate the hypertension, the immediate post-operative effect is very considerable, indeed sometimes dramatic.

Aneurysm of the Renal Artery

This is a rare condition and is often not diagnosed until operation. The commonest symptom is pain. Very occasionally, it has been discovered on X-ray examination during the investigation of a case of hypertension. It will show if calcification has occurred and may be suggested when there is a signet ring appearance on X-ray. The diagnosis can sometimes be confirmed by arteriography. In nearly every case, nephrectomy is necessary, the possible exception being when only a small branch of one renal artery is affected.

Actinomycosis

This rarely affects a kidney. As elsewhere it is characterized by chronic suppuration with marked induration of the organ and of surrounding tissues together with the formation of multiple abscesses leading to sinuses. It may be diagnosed in the early stages when carbuncle of the kidney has been suspected and is operated upon, but as a rule is only established on finding streptothrix from a chronic discharging sinus in the loin. It is rare that surgery can be applied to the treatment. In the early stages a nephrectomy may eradicate the disease but usually it must be treated by an intensive course of penicillin, 1,000,000 units being given daily for a period of 3 or 4 weeks, and iodine by mouth. This treatment may have to be supplemented by a course of X-ray irradiation. If not completely cured, the disease may be sufficiently localized to be treated by nephrectomy.

Infections of the Kidney

Three main types of infection are described as occurring in the kidney: pyelitis, pyelonephritis, and pyonephrosis These conditions may gradually merge into each other.

Pyelitis

This is an inflammation mainly affecting the renal pelvis. The calyces and probably some of the collecting tubules are also involved. The condition can occur in pregnancy, it may be associated with a stone, but most frequently develops without any apparent

tuberculous infection. The tuberculous focus is usually in the spine or in a rib and it is rare to find it in the kidney although it may arise from here.

Signs and Symptoms. In the acute case, pain on the affected side and pyrexia with general malaise are usually present. The tongue is furred, the breath is offensive, and the bowels are constipated. The affected side is tender and there is guarding of the overlying muscles. The normal "waisting" of the loins becomes flattened and in the later stages swelling may occur, producing a definite bulge in the flank. The abscess may point in the Triangle of Petit.

Treatment of Infections of the Kidney. In acute infections of the kidney the most usual causal organism is the B. coli. The patient is often acutely ill and he must be put to bed and encouraged to drink an excess of bland fluids. Many strains of coliform bacilli are sensitive to sulphonamides and the most effective of these are sulphatriad and sulphacetamide. They should be given in a dose of 0·5 grm. 6 hourly, together with an alkaline mixture such as:

Potassium citrate			
Potassium bicarbonate . .	aa	gr.	xxx
Tincture of hyoscyamus . .		m.	x
Aq. chloroform . . .	ad	℥	½

A mid stream specimen of urine in the male or a catheter specimen in the female should be sent for culture and if an organism is grown its sensitivity to sulphacetamide and antibiotics should be determined. In all cases of simple pyelitis improvement occurs quite early on. The temperature will fall, the frequency and dysuria will diminish, and the patient will feel better. If the culture has shown an organism sensitive to sulphonamide, this is continued but should it be insensitive, the treatment is altered. As a general rule, within a week the urine will be free from pus, and will be sterile. Should however, there continue to be infection at the end of 14 days, further investigations must be undertaken and these will include an intravenous pyelogram and probably a cystoscopy. The presence of a stone, or a congenital abnormality producing stasis will be demonstrated and where necessary surgical treatment will be indicated and employed. A chronic infection is at first treated in the same way, but is more likely to be associated with a mechanical cause. The particular therapy will usually depend upon the infecting organism and its sensitivity. The latter must always therefore be tested. The B. coli is usually sensitive to one of the sulphonamides, it is frequently sensitive to mandelic acid, is almost insensitive to penicillin, but usually highly sensitive to streptomycin, aureomycin, terramycin, and chloramphenicol. Staphylococcus aureus and albus are only slightly sensitive to sulphonamide and then probably only to sulphathiazol. They are usually very sensitive to penicillin, streptomycin, aureomycin, and terramycin. Proteus vulgaris and Ps pyocyanea are not sensitive to sulphonamide or to penicillin In vitro mandelic acid will inhibit proteus but it is usually impossible to get the pH of the bladder urine sufficiently low for it to act. Each of these organisms is sometimes sensitive to streptomycin, aureomycin, terramycin or furadantin.

Urinary Tuberculosis

Tuberculosis of the urinary or genital tract is a local manifestation of a general disease, and the primary focus is usually in the chest but may be in the cervical glands or in the mesenteric glands This focus is nearly always quiescent at the time the disease manifests itself in the urinary system. The primary lesion in the urinary tract is generally

disease varies in severity and mild cases undoubtedly go unrecognized, recovery occurring without treatment. If the infection is very severe however, a large necrotic area will form with destruction of this part of the kidney, and there may be marked constitutional disturbance with formation of a perinephric abscess.

Signs and Symptoms. There is usually a history of recurring furunculosis or some other infection and generalized debility. When the carbuncle has become established the patient complains of aching in the affected loin, but this may not be severe. He looks ill, the tongue is furred, the breath is offensive, and the temperature is usually swinging and may be quite high. There is tenderness in the affected loin with muscle guarding which may spread to the muscles of the anterior abdominal wall. The urine may be quite clear but often contains pus and organisms and staphylococcus aureus may be grown on culture. Intravenous pyelogram is as a rule inconclusive, although there may be some irregularity of the kidney shadow with a fluffiness in one area, suggesting extravasation of dye.

Pyonephrosis

In this form of infection, obstruction with dilatation of the pelvis and calyces is also present and the commonest cause of the obstruction is a calculus. The condition is not quite the same as an infected hydronephrosis. It may be limited to a part of the kidney when only one calyx is affected but much more often the whole of the kidney is dilated and contains pus and phosphatic debris. As long as the ureter continues to drain, there may be very little in the way of symptoms but should this cease, the kidney becomes filled with pus, and the clinical condition becomes much more acute. In the chronic form the kidney tissue is gradually replaced with fibrous and lipomatous tissue—fibro-lipomatosis.

Fibro-lipomatosis

This is found in association with infection of the kidney and ureter, more especially when a stone also is present. Minor degrees are seen in most cases of long standing renal calculus, but in the extreme case the kidney may be entirely replaced by a fibro-fatty mass at the centre of which is found a stone.

Signs and Symptoms. There is nearly always a long history referable to the affected kidney, often a stone has already been removed from this side, and there have usually been recurring attacks of pain and fever. Quite often the kidney is palpable and tender on examination. Investigation shows the presence of a calculus and much diminution of the function of the kidney on the affected side. In the chronic case, the urine is always infected and pus may be seen issuing from the ureteric orifice. Should the ureter become blocked, a closed abscess forms and the patient becomes seriously ill. The pain increases on the affected side and there may be rigors with swinging temperature. Should the other kidney also be affected, the blood urea will rise and uræmia develop.

Perinephric Abscess

An abscess may form in the perinephric space following renal or extra-renal infection. It may result from pyelonephritis, pyonephrosis, carbuncle, or calculus obstruction of the kidney. It is sometimes seen after extravasation following rupture of the kidney. Extra-renal causes are: osteitis of the spine, of a rib or of the ilium, communication with an empyema or sub-phrenic abscess, suppuration of para-aortic or psoas glands. Perinephric abscess may be acute or chronic, the latter type being usually associated with a

Signs and Symptoms. It is exceptional for symptoms to occur until the infection has reached the bladder and the most common presenting symptom is frequency of micturition. Occasionally however, a brisk attack of hæmaturia may be the first sign. Increased frequency of micturition occurs in 80 per cent of cases and is present at night as well as during the day. It may at first be slight, but gradually increases and in the later stages becomes so great that there is often nocturnal incontinence, and strangury with continual pain are the unenviable lot of the patient with advanced tuberculous disease of the

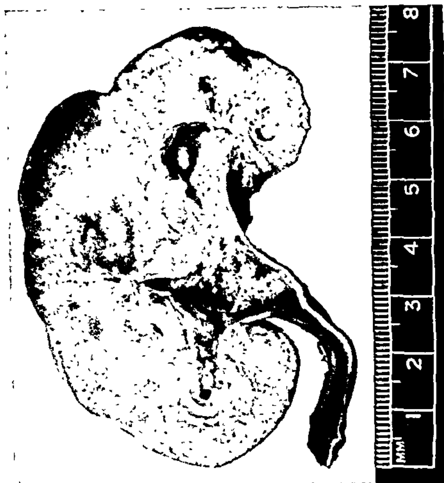


FIG 35 A kidney showing extensive tuberculous infection

bladder. Pain in the loin is not very common and is then chiefly of an aching character. It does not radiate, although if blood clot or tuberculous material is being passed, renal colic may occur. There is little constitutional disturbance from renal tuberculosis.

The findings in the urine are characteristic. There is always pus in an acid urine and usually acid-fast bacilli can be demonstrated. If no organisms are at first seen in such a urine and the cultures are sterile, it is essential that repeated examinations should be made before deciding that tuberculosis is not the cause. It is usual to examine three specimens taken on consecutive days—a mid stream specimen in the male, and a catheter or mid stream specimen in the female—being taken first thing in the morning. The deposit is centrifuged and examined microscopically. If tubercle bacilli are not found after this series of examinations, a culture on a special medium should be set up and/or a guinea pig injected with the centrifuged deposit.

in one of the kidneys. It may result from an embolus of tubercle bacilli, or from reactivation of a latent miliary focus. The lesion ulcerates into a major or minor calyx and reaches the pelvis from which it spreads along the ureter to the bladder. The downward extension may be by direct continuity of tubercles creeping along the lining wall or may be carried in the urine.

Renal tuberculosis is essentially a disease of young adults and presents with greatest frequency between the ages of 20 and 40. Until recently it was thought that the kidney offered little or no resistance to a tuberculous infection but evidence has been brought to show complete recovery and replacement by fibrosis of the tuberculous lesion in many cases. The infection is hæmatogenous and may be single or multiple. The commonest site for its occurrence is in the cortex and the foci here are usually multiple. This is also the commonest site for healing to occur as demonstrated at post-mortem examinations of patients who have died from tuberculosis elsewhere.

A focus may occur in the medulla near the cortex. This is most often single and there appears to be little tendency for this focus to heal. It goes on to ulceration, necrosis, and caseation, and ultimately breaks through into a calyx. The pelvis then becomes infected and its wall is studded with tubercles. The adjacent parenchyma of the kidney is infected and destroyed and ultimately the whole kidney may become involved and be replaced by cavities lined with granulations and containing caseous material and pus. On the capsule there are groups of tubercles and the perinephric fat especially around the hilum becomes matted and adherent. The ureter is affected in the same way as the pelvis and both become thickened, rigid, and dilated. The ureter also becomes tortuous. This tuberculous process is often very chronic and may be present for years before giving rise to symptoms. Very occasionally, the focus appears to heal completely by calcification and occasionally the whole kidney becomes shut off, the ureter stops draining, and a so-called auto-nephrectomy occurs. This closed tuberculosis however, is always a latent focus of infection and may give rise to trouble later.

The Effects on the Bladder. It is most unusual for a patient to present with a tuberculous condition of the kidney until there has been some spread to the bladder. The first common change is œdema of the ureteric orifice on the affected side, and often some tubercles are seen around it. Occasionally, these are first seen at the fundus. As the condition spreads so tubercles appear on the rest of the bladder wall. They coalesce and form an ulcer with irregular, slightly œdematous edges. It is rather characteristic of a tuberculous cystitis that despite areas of ulceration, and tubercles, some parts of the bladder mucous membrane are quite normal. This is never so in an ordinary pyogenic cystitis. With increasing fibrosis and rigidity of the ureter, the orifice becomes drawn up as the result of shortening and it is at this stage that it is described as being "golf-hole" in appearance. Areas of ulceration on the bladder wall heal by fibrosis and this part largely or entirely loses its power of distensibility. Ultimately the whole wall becomes very contracted, calcification very occasionally occurs and there is marked diminution in the capacity of the bladder, in part from spasm and in part from fibrosis. A bladder such as this, may be ruptured during irrigation if too high a pressure is used.

Tuberculous Bacilluria. It used to be considered that a normal kidney could excrete tubercle bacilli but this has been disproved by Medlar (1924) and Band (1943) In an extensive series of cases, it was always possible to demonstrate a focus, although this was sometimes very small.

days. During the next fortnight 7 gms. of Para-amino salicylic acid is given three times daily. These two fortnightly courses alternate for 6–12 months.

After the patient has been under treatment in hospital for one month, an assessment is made as to the necessity for and timing of surgical intervention. If there is any pulmonary activity, surgery in the urinary tract is delayed until this has been controlled. If at the end of a month however, the active lesion is apparently localized to one kidney and is of an extent which is not likely to heal, a nephrectomy is undertaken. If the lower end of the ureter shows obvious changes with dilatation and rigidity, the whole of the ureter should be removed and this will involve a separate incision to reach the lower end. If however, there are no obvious changes radiologically or endoscopically and at operation it appears macroscopically normal, the whole of it need not be removed but only as much as can be reached through the nephrectomy incision. If there is an active lesion in a single kidney, partial nephrectomy should be contemplated. This operation is being done with a considerable degree of success especially in Sweden and some surgeons advocate this limited attack even when one kidney is apparently normal. After the active renal focus has been removed, the infection of the bladder usually heals and frequency returns to normal or materially diminishes. In some cases however, during the process of healing, much fibrosis occurs and the bladder capacity greatly diminishes. The frequency may become intolerable or the remaining ureter and pelvis become greatly dilated. In the absence of active tuberculosis much relief may be obtained by a uretero-colic anastomosis or by establishing a cutaneous ureterostomy. Recent work suggests that relief may be obtained if the bladder is enlarged by anastamosing to it a loop borrowed from the lower end of the ileum and excluded from the alimentary tract.

BLADDER

Congenital Anomalies

In the early embryo, the major portion of the bladder is formed from a diverticulum of the cloaca, the allantois, which ends blindly in the body stalk, and by the end of the second month, the subdivision of the cloaca into urogenital and alimentary components is completed. A mesodermal shelf on the ventral aspect of the hind gut grows distally to form the uro-rectal septum and finally meets the cloacal membrane and the urogenital sinus and rectum become separately defined. The allantois normally becomes obliterated as mesoderm continues to be laid down between the cloacal membrane and the body stalk; this forms the anterior wall of the bladder, and from condensation within this mesoderm, the symphysis pubis is developed. Meanwhile, the mesonephric ducts with ureteric buds have continued to develop and whilst for a time, there is a single excretory duct on each side, by differential growth this common channel is taken into the wall of the vesico-urethral canal so that on each side the openings of the ureter and mesonephric duct come to lie at a distance from each other.

Anomalies are all rare. If that part of the allantois which stretches from the umbilicus to the cord is not obliterated and remains patent, a fistula—urachal—is present. If the bladder part remains open there is a congenital diverticulum. If it remains patent through most of its length, but closed at both ends, a urachal cyst forms. If fusion of the ventral mesoderm fails to occur, there is an extrophy or ectopia of the bladder (*see* Fig. 36).

An X-ray examination may reveal or confirm the presence of a tuberculous infection (*see* Fig. 35) Early signs on excretion urography are flattening of the normally cupped calyx with some dilatation. Later the calyx becomes rounded, irregular, and knobbly and when ulceration has occurred it becomes grossly deformed. Small areas of calcification are often seen in the kidney and many simulate stones. The irregularity of the edge and the position in the cortex, should suggest the correct diagnosis. Calcification is no indication that the condition is quiescent. When spread has occurred to the calyces and pelves, these become dilated and there is stasis. There may be diminished or complete absence of excretion on the affected side. When spread has occurred to the ureter, this becomes dilated and tortuous and stasis is a characteristic feature.

Differential Diagnosis. The diagnosis of urinary tuberculosis is established when acid-fast bacilli are found in the urine. A centrifuged deposit is examined after a Ziehl-Naelsen stain. The only possible doubt which can arise is whether there has been contamination with the smegma bacillus. If tuberculosis is suspected and bacilli are not seen, one or two other conditions may give rise to some doubt (Bilharzia—*see* p. 81).

Abacterial Pyuria. This is a condition in which the whole of the bladder may be affected by inflammation or there may be inflammation of the urethra or both. The symptoms are much the same as tuberculous cystitis but on cystoscopy no tubercles are seen, the whole of the wall is affected and as a rule there are no changes in the upper urinary tract on radiological examination.

Hunner's Ulcer. This condition of localized interstitial cystitis is confined to women, usually in the late 30's although it may occur earlier. The urine does not contain pus; cystoscopy is almost always impossible without a general anæsthetic, the bladder capacity is extremely small; most of the mucous membrane seen appears normal, but in one or probably two areas there is a small ulceration with radiating sub-mucous fibrosis. On distension of the bladder with an irrigating cystoscope the ulcerated area will be seen to start oozing blood after distension commences.

Treatment. The treatment of Tuberculosis of the Genito-urinary tract has been greatly altered since 1944. The discovery of Streptomycin gave us a specific remedy to the infection. Surgical intervention has become less often necessary, has become less drastic, and quite often much can be done to help a case which would have previously been considered hopeless. The diagnosis of tuberculosis is made by identifying the M. tuberculosis in the urine The extent of the disease is demonstrated by radiological and endoscopic examination If there is marked interference with function and obvious calcification shows on intravenous pyelogram, it is unlikely that the condition will clear up without surgical intervention but if the lesion is small or not apparent radiologically, operation will not be necessary. When diagnosis has been established the patient should be admitted to hospital and a sanatorium regime instituted. Specific treatment, according to Latimer of the Presbyterian Hospital, New York, should be started as soon as the diagnosis is established He has had a wide experience in dealing with the disease in ex-service men and in this group has achieved remarkable success Streptomycin 1 gm. is given twice weekly, and 300 mgs of isoniazid and 15 gm. of calcium Para-amino salicylic acid are given daily in divided doses.

The details of drug administration advised by Cosbie Ross, Gow and Hill, are different, more involved and do not appear quite so rational. The treatment is arranged in fortnightly courses—Streptomycin 2 gms. and isoniazid 250 mgs. are given daily for 14

The anterior wall of the bladder, the anterior part of the abdominal wall, and the roof of the urethra are all missing, the pubic bones with the recti abdominalis muscles are widely separate (*see* Fig. 37), and the trigone with the ureteric orifices can be seen at the lower end of the exposed bladder.

Treatment. If a urachal fistula is present, the track is excised and a repair performed. If any other abnormality of the allantois tract gives rise to symptoms, e.g. cyst formation, it should be excised. Ectopia vesicæ is rarely, if ever, helped by conservative plastic procedures. A uretero-colic anastamosis should be performed. This is probably best done in two stages, after the child has normal rectal control, say between the ages of two and three years. The bladder should be removed as metaplasia of its mucous membrane always occurs and there is probably an increased tendency to the occurrence of malignant disease.

Injuries of the Bladder

Open Injuries

These are rare in civil life, but not uncommon in wartime. They may be due to stab or missile wounds and are nearly always complicated. The pelvis is frequently fractured and the rectum or colon also involved. The diagnosis is suspected from the direction of the track of the wound and is confirmed if urine leaks from the wound. Treatment is in accordance with general principles and the details in reference to the bladder will depend on the extent of the damage. It is usually possible to conserve the organ, and after the edges of the rupture have been excised and sutured, the bladder is drained suprapubically, except in minor injuries. Osteitis of the pubis is a fairly common complication.

Closed Injuries

These are quite uncommon and probably always accompany a full bladder. Two forms are described depending on whether the tear is intra- or extra-peritoneal.

Intra-peritoneal Rupture. This is generally associated with a blow on the lower abdomen, when the bladder is moderately full. A sudden severe pain is felt usually accompanied by nausea and a feeling of faintness. The pain gradually becomes less and the condition of the patient improves for a time provided there is no infection in the urine. The lower abdomen is tender with some guarding but rigidity is not a pronounced feature. Bowel sounds are usually absent from the beginning. If the tear is small, the patient may pass some urine which is blood stained. Without treatment the general condition deteriorates, the abdomen becomes distended, and a paralytic ileus develops.

If rupture is suspected the patient should be prepared for laparotomy and taken to the theatre. A catheter is passed and this should enter the bladder without difficulty. Blood stained urine is an indication of injury. A measured amount of sterile water or normal saline is then slowly injected into the bladder and the amount withdrawn should be the same quantity as that introduced. If there is a considerable deficiency in the amount recovered, rupture is likely. An opaque fluid may be injected along the catheter and an X-ray taken. A rupture will be shown by extravasation.

Extra-peritoneal Rupture. This is usually associated with a fractured pelvis although in the latter condition a tear of the prostatic urethra is much more common. The differential diagnosis is not always easy and may not be determined until operation. There is



Fig. 36. Ectopia vesicæ in a girl of five years



Fig. 37. The typical separation of the pubes in ectopia vesicæ

The anterior wall of the bladder, the anterior part of the abdominal wall, and the roof of the urethra are all missing, the pubic bones with the recti abdominalis muscles are widely separate (*see* Fig. 37), and the trigone with the ureteric orifices can be seen at the lower end of the exposed bladder.

Treatment. If a urachal fistula is present, the track is excised and a repair performed. If any other abnormality of the allantois tract gives rise to symptoms, e.g. cyst formation, it should be excised. Ectopia vesicæ is rarely, if ever, helped by conservative plastic procedures. A uretero-colic anastamosis should be performed. This is probably best done in two stages, after the child has normal rectal control, say between the ages of two and three years. The bladder should be removed as metaplasia of its mucous membrane always occurs and there is probably an increased tendency to the occurrence of malignant disease.

Injuries of the Bladder

Open Injuries

These are rare in civil life, but not uncommon in wartime. They may be due to stab or missile wounds and are nearly always complicated. The pelvis is frequently fractured and the rectum or colon also involved. The diagnosis is suspected from the direction of the track of the wound and is confirmed if urine leaks from the wound. Treatment is in accordance with general principles and the details in reference to the bladder will depend on the extent of the damage. It is usually possible to conserve the organ, and after the edges of the rupture have been excised and sutured, the bladder is drained suprapubically, except in minor injuries. Osteitis of the pubis is a fairly common complication.

Closed Injuries

These are quite uncommon and probably always accompany a full bladder. Two forms are described depending on whether the tear is intra- or extra-peritoneal.

Intra-peritoneal Rupture. This is generally associated with a blow on the lower abdomen, when the bladder is moderately full. A sudden severe pain is felt usually accompanied by nausea and a feeling of faintness The pain gradually becomes less and the condition of the patient improves for a time provided there is no infection in the urine. The lower abdomen is tender with some guarding but rigidity is not a pronounced feature. Bowel sounds are usually absent from the beginning. If the tear is small, the patient may pass some urine which is blood stained. Without treatment the general condition deteriorates, the abdomen becomes distended, and a paralytic ileus develops.

If rupture is suspected the patient should be prepared for laparotomy and taken to the theatre. A catheter is passed and this should enter the bladder without difficulty. Blood stained urine is an indication of injury. A measured amount of sterile water or normal saline is then slowly injected into the bladder and the amount withdrawn should be the same quantity as that introduced. If there is a considerable deficiency in the amount recovered, rupture is likely. An opaque fluid may be injected along the catheter and an X-ray taken. A rupture will be shown by extravasation.

Extra-peritoneal Rupture. This is usually associated with a fractured pelvis although in the latter condition a tear of the prostatic urethra is much more common. The differential diagnosis is not always easy and may not be determined until operation. There is



FIG. 36. Ectopia vesicæ in a girl of five years.



FIG 37. The typical separation of the pubes in ectopia vesicæ

The anterior wall of the bladder, the anterior part of the abdominal wall, and the roof of the urethra are all missing, the pubic bones with the recti abdominalis muscles are widely separate (*see* Fig. 37), and the trigone with the ureteric orifices can be seen at the lower end of the exposed bladder.

Treatment. If a urachal fistula is present, the track is excised and a repair performed. If any other abnormality of the allantois tract gives rise to symptoms, e.g. cyst formation, it should be excised. Ectopia vesicæ is rarely, if ever, helped by conservative plastic procedures. A uretero-colic anastamosis should be performed. This is probably best done in two stages, after the child has normal rectal control, say between the ages of two and three years. The bladder should be removed as metaplasia of its mucous membrane always occurs and there is probably an increased tendency to the occurrence of malignant disease.

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pain and tenderness in the suprapubic region with guarding. The urine—if it has been passed—is blood stained. There is no blood apart from micturition at the external meatus as is fairly common with a urethral injury. X-ray after the injection of an opaque fluid will show a leak. If suspected, the bladder is exposed and any tear identified and sutured. It is usually necessary to drain the bladder suprapubically.

Instrumental Injury. This may occur at the time of resection of a bladder growth when the McCarthy resectoscope is being used. It may be produced with a diathermy electrode or a Kidd's diathermy cystoscope. If accurate visibility is always obtained, such a complication should not occur. Rupture has happened if a Bigelow's evacuator has been used where a bladder is sacculated. The sudden increase in intra-vesical pressure is too great for the thinned out wall to remain intact. The site of the injury depends on the position of the sacculations, but usually this is extra-peritoneal.

The day after operation or a few hours after the removal of a urethral catheter, the patient complains of pain suprapubically low down on either side. There is an elevation of temperature; there is tenderness with some guarding on abdominal palpation and on rectal examination an area of tenderness which may be a little boggy, is often felt with an examining finger. If the nature of the operative procedure has made a leak possible, or probable, an abdominal incision should be made on the affected side and a rubber drain introduced paravesically to the site of rupture. At the same time a catheter should be introduced and fixed in the urethra. It should remain there until at least 48 hours after the temperature has settled.

Fistula of the Bladder

Vesico-colic and Recto-vesical

Congenital Fistula. Congenital fistula between the bladder and rectum are nearly always associated with imperforate anus and this is the more important aspect of the case.

Traumatic Fistula. In the male, this may occur as the result of a missile wound and rarely follows operation. The rectum has been injured in prostatectomy, especially when a radical excision has been performed either through the perineal or retropubic approach and this has also occured during gynæcological procedures.

Signs and Symptoms. If the communication is large the condition is obvious and urine comes from the rectum. A severe cystitis may develop requiring urgent treatment. If the fistula is small, there may not be much in the way of disturbance; a little urine may come out via the rectum and there may be periodic attacks of cystitis.

Inflammatory Fistula. Diverticulitis of the colon is the commonest cause of spontaneous vesico-colic fistula, although it does occur in association with colitis and regional ileitis. It has also followed a tuberculous enteritis.

Signs and Symptoms. There is often very little in the history to suggest a lesion of the bowel and the symptoms are then concentrated on the bladder. The opening is usually small and there may not be a constant communication between the two viscera This will then give rise to alternating periods of cystitis and periods when the bladder function appears normal. Quite often the patient will observe that very soon after the onset of frequency, the urine becomes quite thick and offensive and in a significant percentage of cases, there is bubbling or the obvious passage of air along the urethra. On close questioning some disturbances of bowel habit are nearly always to be elicited. On examination, the urine is found to be heavily infected, usually the infection is mixed and B. coli

and Streptococcus fæcalis are commonly present. There may be lower abdominal tenderness but it is not usual to feel any definite mass in the recto-vesical pouch. At cystoscopy, the bladder opening of the track can often be identified. It is usually high up on the back wall and appears as a dark recess surrounded by an irregular area of redness and œdema. Very occasionally, a few bubbles of air may be seen to enter the bladder and sometimes a cloudy influx can be seen coming from this recess.

Treatment of Traumatic Fistula. In all but the minor case, a colostomy should be established. A third of the traumatic cases appear to heal spontaneously (Wyndham, 1948) and a suprapubic cystostomy to which continuous suction drainage is applied, helps this. If the fistula persists, it is exposed through the perineal route, the rectum being separated from the back of the urethra and bladder. This opening into the bladder is then excised and the freshened edges sutured in two layers. The mucous membranes of the rectum surrounding the fistula and distal to it is excised as far as the anal margin, the upper edge is pulled down and is sutured to this anal margin without tension.

Treatment of Inflammatory Fistula. If, as is usually the case, the fistula is due to diverticulitis of the colon, the affected segment of bowel will almost certainly have to be removed. If the patient is fit, this should be done at the first operation. Otherwise a preliminary colostomy which is usually in the transverse colon, will be necessary as a first stage. Later the loop of bowel is dissected off the back of the bladder and removed.

Neoplastic Fistula. Rarely a carcinoma of the bowel becomes attached to the bladder and ulcerates into it. Even less commonly does a carcinoma of the bladder ulcerate into the bowel. In either case, the growth may be small and removable. A colostomy has usually to be established although it may be only as a temporary procedure, and the appropriate parts of the bladder and bowel are removed. If, as is more likely, a large part of the bladder has become involved a total cystectomy may be necessary. Should removal of the lower bowel and bladder both be required, an artificial reservoir can be fashioned from a dysfunctioned loop of ileum, implanting the ureters into this and bringing one end of the bowel out through the abdominal wall. This appears to be greatly preferable to a "wet colostomy."

Vesico-vaginal Fistula

This occurs in three sets of circumstances. (*a*) Obstetrical and following vaginal operation; (*b*) following intra-peritoneal pelvic operations; and (*c*) in association with carcinoma of the uterus, with or without radium treatment.

(*a*) As the Result of Obstetrical or Vaginal Injuries. Prolonged delay in the second stage of labour may lead to long continued pressure on the bladder between the fœtal head and the back of the pubis and necrosis with fistula may follow. The fistula is always low down in this type of case, and may be on the trigone and involve the urethra. Very occasionally, the bladder is injured in doing a colporrhaphy or pelvic floor repair. Here again the site of injury is low down, just above or on the trigone.

(*b*) Following Intra-pelvic Operations. The bladder may be very thin-walled and indefinite and during a hysterectomy, when the anterior peritoneal reflexion is being divided, is in danger and may be opened. As a general rule no ill comes of this if it is carefully re-sutured. Such is not always the case and a vesico-vaginal fistula may develop. In view of the position of the injury, the communication is high up in the vagina and often on the postero-superior surface of the bladder

(*c*) FISTULA FOLLOWING NEOPLASMS and especially neoplasms of the uterus may arise anywhere. It usually occurs to one side however, and may cause an obstruction of a ureter at the same time. It may follow on treatment of carcinoma of the cervix by radium.

Signs and Symptoms. A patient with a vesico-vaginal fistula is always wet. The degree of wetness will depend on the size of the opening. If large, little or no urine will be retained in the bladder; there will be complete incontinence and she will be constantly wet. At the other extreme, is the case with a very small opening when the patient is usually damp especially when walking about, but at the same time quite a lot of water is passed normally. On careful examination of the vagina, however small the fistula, it should be seen and if the vagina is mopped dry and pressure applied to the suprapubic region, a trickle or gush or urine can be seen entering the vagina through the puckered opening. The fistula may lie on the anterior vaginal wall or high up in the anterior fornix. If the opening is a small one and the patient voiding a good quantity of urine, the differentiation between uretero-vaginal fistula arises. A cystoscope should be passed and the bladder opening can then be seen and usually accurately identified. If in doubt, a catheter is passed along each ureteric orifice, and if the fistula is vesical it should go without difficulty. If a doubtful small opening is seen in the bladder, a catheter is passed through this and in the case of a vesico-vaginal fistula, the tip of the instrument will appear in the vagina. In a fistula, following a carcinoma of the cervix treated by radium, it may be difficult to decide whether the opening is neoplastic or due to radiation necrosis and a biopsy may be necessary.

Treatment. In the majority of cases of vesico-vaginal fistulæ which can be cured, the operation can be done through the vaginal approach. The low obstetrical injuries are approached in the same way as those following a vaginal operation. The vaginal orifice of the fistula is excised and the bladder is separated from the anterior vaginal wall. The openings in the two structures are closed in layers and preferably at a different level. If small, the bladder opening may be closed by a purse string suture. The bladder should be continuously drained by an indwelling urethral catheter. If the internal urethral sphincter is involved in the fistula, attempts to repair it and produce continence more often fail. Such a case usually ends in a uretero-colic anastomosis but some success has been claimed for refashioning a urethra or dividing the old one just distal to the internal urinary meatus, and implanting the urethra in a tunnel which passes through or just behind the interureteric bar. If the fistula has followed an intra-pelvic operation such as a hysterectomy, the opening is high and lies at the apex of the vaginal or anterior fornix. Where it is large, access from the vagina is difficult and in most hands a transvesical approach is safer and more certain to produce a cure. The bladder is opened; the peritoneum is reflected from its upper surface by dissection and the line of incision passes down to, and includes the internal opening of the fistula The peritoneum and vaginal wall are fairly widely cleared from the back of the bladder and the opening in the vagina excised and sutured. The bladder is then closed in layers and drained through a urethral catheter. This provides better drainage than a suprapubic tube and the bladder can be kept empty.

Suprapubic Fistula

This has always been preceded by a wound of the bladder and in most cases this has been a surgical wound. The fistula may be intentional or unintentional.

An Intentional Suprapubic Fistula is done when the patient is unable to empty the bladder normally and the cause of this inability cannot be removed. It is performed in men with prostatic obstruction, who are not fit or refuse to have the obstruction removed. It may be performed in certain rare cases when the urethra has become so occluded by stricture that no instrument can be passed. It is done in certain neurological conditions when there is retention with infection and it may have to be done when malignant disease either from the bladder, rectum, or prostate produces obstruction which cannot be relieved in any other way. A tube is introduced along the fistula and drains the bladder. There are two main types of tube; one is self-retaining, e.g. Malecôt, de Pezzer, or Foley, and is usually controlled by a clamp or spigot at the outer end. This can be released by the patient or nurse when there is the desire to pass water. Such a tube is changed at intervals of 2–4 weeks depending on the amount of phosphatic deposit and debris which collects and occludes its lumen. The other type of tube is the St. Peter's pattern. It is straight, with an opening at the end and one at the side. It slips easily into the bladder and is retained in position by a rubber flange which grips it and which in turn is held against the abdominal wall by a belt. This tube drains into a rubber bag which lies along the thigh when the patient is ambulant. This type of tube can be easily changed and this should be done daily or every other day, the bladder being irrigated at the same time. The bladder can be kept cleaner with this type of tube than with a self-retaining one, but it requires considerably more apparatus.

Unless the opening of the fistula is at least 2 in. above the symphysis, it is apt to leak and is uncomfortable. Permanent suprapubic drainage is always avoided if at all possible, as a high proportion of patients are miserable and barely tolerate it. Should the tube inadvertently come out and not be replaced the fistula rapidly closes down and within a few hours the original tube cannot be replaced. The fistula must then be dilated and Wyndham Powell's straight graduated dilators are the best for this purpose.

Unintentional Suprapubic Fistula. This follows injury or a surgical operation during which the bladder has been opened. After accidental injury to the bladder, the cause of persistent fistula is usually a foreign body such as a necrosed fragment of the pubic bone or an unabsorbable suture.

Post-operative causes are:

(1) Obstruction at the internal meatus or prostatic fossa by flap, fibrosis, or prostatic remnant.

(2) A diverticulum of the bladder whose presence has been overlooked at the time of the original operation.

(3) When part of the membraneous urethra has been pulled up and removed at prostatectomy, a stricture usually forms. This is more likely to occur at retropubic prostatectomy.

(4) Prolapse of the bladder through the wound, which may occur after transvesical prostatectomy when the opening necessary for a large Marion's tube does not contract quickly. The vesical mucous-membrane is a rather brighter red than is granulation tissue.

(5) The bladder may become adherent to the back of the symphysis pubis.

(6) After prolonged preliminary drainage an epithelialized track forms and may not have been removed.

Treatment. A persistent fistula must be carefully investigated. A cysto-urethroscope should be passed and the bladder wall, bladder *neck*, and prostatic bed or urethra

inspected. If obstruction is the cause, the canal is usually quite narrow and it may not be possible to pass an instrument along the urethra into the bladder. It may be possible to see the opening through the pan-endoscope and slit it with a Collings' diathermy knife and thus find a way in. If this is not possible an attempt should be made with a Phillip's filiform guide and if this succeeds the urethra is fully dilated before inspection. If the obstruction is at the bladder neck, it is usually best dealt with by the McCarthy resectoscope. If it is not possible to pass an instrument, the bladder must be opened and the obstruction removed under direct vision. If distal to this, intermittent full dilatation should allow the fistula to close.

A diverticulum of the bladder should be excised. This may be a most difficult and tedious procedure as a secondary operation, especially with a fistula present.

If the bladder mucous membrane has prolapsed, if the wall is adherent to the back of the pubis, or if there is an epithelialized track, the opening of the fistula is excised, the bladder is mobilized, closed in two layers by a continuous stitch, and drained through a urethral catheter for 10 days.

Fistula of the Vas Deferens. This may occur when the vas has been divided as a precaution against epididymo-orchitis and has also been described as occurring in association with genital tuberculosis.

Treatment. The fistula is excised, the vas dissected as far as the internal ring, divided and ligatured.

Infections

Cystitis

Inflammation of the bladder or cystitis is a condition which occurs at all ages in either sex, but is more common in the female, especially in childhood, at puberty, on marriage, and during pregnancy. It is described as occurring in three forms—acute, chronic, and recurrent.

Acute Cystitis

Ætiology. The commonest cause of acute cystitis is infection with Bacillus coli; less commonly, Streptococcus fæcalis, Staphylococcus aureus, and Staphylococcus albus are found. Prior to effective chemotherapy in the treatment of gonorrhœa, an acute cysto-prostatitis sometimes complicated this disease. The onset of acute cystitis is usually quite sudden; there may be a premonitary period of malaise lasting 12–24 hours, but this is unusual Occasionally the patient complains of having caught a chill during the previous 48 hours. When an infection occurs a few days after marriage it is often referred to as "honeymoon pyelitis" although it is usually an acute cystitis. Exhaustive search nearly always fails to reveal a gonococcal infection and the causative organism is usually B. coli. It is probably due to the trauma of coitus although another factor may be alteration in the bowel habit because of the sudden change in habits and regime.

Pathology. The mucous membrane of the whole of the bladder becomes reddened, congested, and œdematous. There may be areas which are more involved than others, but the whole bladder is affected in an acute non-specific cystitis At certain points the mucous membrane may give way, slough, and produce an acute ulcer. At others, there may be sub-mucous hæmorrhages either patchy or petechial.

Symptoms and Signs. The patient may complain of having been "out of sorts" for a day or so but often the first thing noticed is a sudden increased desire to pass water. Within a few hours pain is usually a common feature. There is burning along the urethra during and pain referred to the tip of the penis at the end of the act of micturition. The frequency often increases so much that there is a constant desire to void. Hæmaturia is often an important symptom. In some cases it is out of proportion to the discomfort and increased frequency and may then be the predominating feature. It may suggest that cystoscopy is essential as an early investigation. On examination the patient usually looks quite well, and has no constitutional manifestation of the infection. There may be a raised temperature however, with the tongue furred and the face flushed. If urinary infection is the cause of this, it is likely that the upper urinary tract is also involved. There may be some suprapubic tenderness. Examination of the external genitals shows nothing abnormal, but rectally there is almost always tenderness of the bladder. The urine is hazy or turbid, it may contain blood macroscopically. The centrifuged deposit shows pus cells, organisms, and usually red blood cells.

Treatment. At this stage, cystoscopy is neither necessary nor advisable, and if the urine appears to be infected, a clean specimen—mid-stream in the male and catheter in the female—should be collected and sent to the laboratory for culture and for sensitivity tests of any organisms found. Treatment should be instituted immediately. The following:

Potassium citrate			
Potassium bicarbonate .	aa	gr.	xxx
Tincture hyoscyamus		m	x
Aq. chloroform .	ad		½ oz.

should be given 6 hourly together with sulphacetamide or some other soluble sulphonamide: 1 gm. 6 hourly for 2 days and then 0·5 gm. 6 hourly for 5 days. Copious bland fluids are given by mouth, the traditional barley water being as good as any. Such a regime clears up most cases and the symptoms quickly abate. Should this not be the case however, the result of the sensitivity tests will be at hand, and an appropriate remedy employed.

Recurrent Cystitis

This is a clinical rather than a pathological entity. It occurs much more commonly in women than in men. The patient gives a history of recurring attacks of acute cystitis. The causative organism is usually the B. coli, but may be Streptococcus fæcalis, or Staphylococcus aureus Such a case may result from an infection in the bladder never completely irradicated, but in many cases there are intervals when the urine is sterile for a period and suddenly the clinical manifestations of acute cystitis develop and the bladder is again found to be infected without any obvious cause Then careful investigation becomes necessary to discover some latent focus. In the female, this may be from a gynæcological focus such as a cervicitis or an erosion. It has been suggested that it is frequently due to polyps or mucus tags around the internal meatus. In the male, the focus is most commonly found in the prostate. In some cases however, even after careful and exhaustive search no focus can be demonstrated in or out of the urinary tract.

Treatment. If a focus of infection is found it should if possible be irradicated.

If this cannot be effected, each fresh attack of cystitis should receive appropriate treatment.

Chronic Cystitis

This is an infection of the bladder which has been present for a long time. There is usually some cause other than the infecting organism which makes irradication difficult or impossible and the most common of these is obstruction either at the bladder neck, from the prostate, or in the urethra.

Chronic cystitis also occurs in the aged without any apparent obstructive lesion. It quite often follows on an acute or subacute cystitis and can complicate vesical calculus and carcinoma of the bladder. Various types of cystitis have been described but they are often degrees of the same condition and one or more may be seen in the same case. In *phlegmonous cystitis* variable areas of the mucous membrane become devitalized and slough. This gives rise to the *ulcerative cystitis.* The term bullous cystitis is used when multiple blebs appear, usually in ordered rows and especially near the internal meatus. These are best seen on profile at cystoscopy. Some areas are covered with a phosphatic deposit, some of which is stirred up on irrigating the bladder, and then the inside medium resembles a snow fall. Any organism found in acute cystitis may occur in chronic disease but the infection is often mixed and proteus vulgaris, or pyocyaneus are frequently found.

Treatment. This may be extremely difficult. Any obstructive cause or other factor such as stone, growth, or diverticulum should be removed and the appropriate remedy administered. Even when it is known that there is a considerable amount of residual urine, it may not be possible to remove the obstruction, or none may be demonstrable. Bladder irrigation through a catheter or suprapubic cystostomy may help. Lotions such as Oxycyanide of Mercury 1:6000—Sodium Hyperchlorite 1:10,000—Silver nitrate 1:2000 and Flavine 1·1000 have all helped. Where there is phosphatic encrustation Zuby's solution G may be beneficial.

Abacterial Cystitis

Abacterial urethritis is only very rarely encountered. A small group of cases of pyuria with cystitis but without urethritis are found to be abacterial after repeated investigation. The condition may be acute or gradual in its onset and may be preceded by a typical attack of acute cystitis from the Bacillus coli, which has become sterile on treatment It is commoner in the male than in the female. It is almost certainly due to a virus infection.

Symptoms and Signs. Frequency of micturition is the principal symptom and there is an almost constant desire to pass water, both day and night. Abdominal examination shows a little tenderness in the bladder region suprapubically and per rectum, and the urine contains pus but repeated examinations show no organisms, and cultures are sterile. The condition must be differentiated from Tuberculosis and Bilharzia and in the female from chronic interstitial cystitis or Hunner's Ulcer. On cystoscopy, there is nothing typical in the acute phase. The bladder may be red and œdematous and is extremely intolerant, even under full anæsthesia.

Treatment. Prior to the introduction of antibiotics this was extremely difficult. Aureomycin usually clears up the condition in 48 hours, but if it should fail, intravenous arsenic (Novarsenobillon) 0·5 grm given three times at weekly intervals may help.

Hunner's Ulcer or Chronic Interstitial Cystitis

This condition is a localized interstitial cystitis which occurs exclusively in women usually towards the menopause, but may begin as early as at 22 years of age.

Pathology. This has not been properly elucidated. It is an inflammation affecting the muscle wall rather than the mucous membrane and produces a very severe disability without an extensive cystoscopic lesion. Some cases begin with an acute cystitis from a B. coli infection but when this has been rendered sterile, the symptoms are not relieved. Biopsy of the affected area shows a simple inflammatory reaction.

Symptoms and Signs. The chief complaint is frequency of micturition but there is also pain in the bladder region which is nearly always present for some, if not most of the day. This pain is not associated with micturition, nor is it relieved by it. It is sometimes referred to the external urinary meatus. Most of the time the urine is crystal clear and contains no abnormality. On cystoscopy, the bladder capacity is smaller, usually not much more than 50 c.c. (2 oz.) Most of the bladder wall and both ureteric orifices appear normal, but on the postero-lateral wall on either and sometimes on both sides, there is a small ulcer with submucous fibrous ridges radiating from it. If the bladder is distended under vision, the ulcerated area stretches and begins to ooze blood.

Treatment. There is no sure cure. Diathermy of the ulcerated area, stretching of the bladder, injection of cortisone around the ulcer, alphatocopherol in large doses, have all been claimed to help. Partial cystectomy does not seem to help and some cases require uretero-colic anastomosis before relief is obtained. If the ulcer has healed and a small permanently contracted bladder remains, relief has been obtained by anastomosing a loop, borrowed from the lower end of the ileum, to the bladder.

Bilharzia

This infestation is endemic in the greater part of Africa, throughout Palestine, Syria, Aden, Arabia, Iran, and Iraq. It is also met with in parts of Portugal, Greece, Cyprus, Mauritius, and Madagascar. The species which affects the urinary tract is the Schistosoma hæmatobium. The female lays her eggs in the smallest submucous venules of the bladder, and if the ova develop, they pass through the mucous membrane of the bladder to be voided in the urine.

Symptoms and Signs. The first sign of involvement of the urinary tract is usually hæmaturia, which occurs because of the extrusion of the ova. As the disease develops, so does cystitis with frequency, dysuria, and occasional hæmaturia. The diagnosis is established on finding Bilharzia hæmatobia in the urine, but the stage and extent can only be determined cystoscopically. There are five main lesions seen:

(1) A Bilharzial tubercle
(2) A Bilharzial nodule.
(3) A Bilharzial papilloma.
(4) A Bilharzial ulcer.
(5) A neoplastic papilloma.

A Bilharzial tubercle, which is an aggregation of ova, to some extent resembles a collection of tubercles. When the tubercles coalesce, they form a second lesion which is a Bilharzial nodule. This is rather grey in colour and resembles pearls of barley lying deep to the mucous membrane. A Bilharzial papilloma is a dark red excrescence standing out from

the mucous membrane and the lesion is usually multiple. A Bilharzial ulcer is single and probably malignant. The last lesion is a true neoplastic papilloma with short irregular fronds. Calcification in the bladder wall is common.

Treatment. This is by antimony salt in the earlier stages. Sodium antimony tartrate is given every second day starting with gr. ½ and increasing by gr. ½ every second day, up to gr. 2½. A total dose of gr. 20 is administered in one course.

When a definite neoplasm has developed, total cystectomy is usually the only line of treatment which can be pursued.

Actinomycosis

This very occasionally attacks the urinary tract when either kidney or bladder may be affected. The diagnosis is usually only suspected in long standing infections and may be made by finding streptothrix in the urine, or pus from the loin.

Treatment is by penicillin 1,000,000 units given daily, together with iodine by mouth and if there is delayed resolution X-ray irradiation should be tried.

Tumours of the Bladder

New growths are found comparatively frequently in the urinary bladder, and more often in men than in women. The large majority of these tumours are epithelial, and more than half are malignant both histologically and in their behaviour. Even where the tumour is histologically benign and can be readily destroyed with diathermy, the outlook is not always as for other benign tumours, since another villus papilloma is liable to form in the bladder after a variable lapse of time and in some instances this new tumour may be malignant.

Epithelial Tumours

In the large majority of cases there is no apparent cause for the development of these growths. They are more prone to occur in aniline dye workers and are then thought to be affected by the benzidine and beta-naphthylamine excreted in the urine. The only other recognizable cause is Bilharzia and this undoubtedly predisposes to the formation of a neoplasm of the bladder which is usually a carcinoma. Recent work suggests that certain enzymes are found in greater concentration in the urine of individuals who have formed tumours of the urinary tract.

Benign

This is a transitional cell villus papilloma, and in its simplest form consists of a stalk of vessels and connective tissue which branches like a conifer. Both the stem and its branches are covered with transitional epithelium similar to that of normal bladder mucous membrane. It is quite unusual to find a single frond, and much more commonly there are several which come together at the root and have the appearance of red seaweed or a sea anemone with its fimbriæ gently waving about in the water. Sometimes there are many fronds quite closely packed and the tumour looks more fleshy and rather like a half ripened raspberry. Secondary benign papillomata—often multiple—usually consist of numerous short fronds, a little redder in colour than the normal bladder.

Primary villous tumours are most commonly found in the bladder wall within a centimetre or two of a ureteric orifice. Secondary tumours may be found anywhere and

occasionally are seen in the prostatic urethra. A primary papilloma is more often single but there may be multiple growths present when first seen. A careful search must always be made so that none are overlooked.

The Progress of a Benign Bladder Growth. A tumour which is histologically benign may behave in one of three ways.

(1) A single growth may be easily destroyed by diathermy and not recur, or at any rate the bladder remains clear for many years.

(2) A single growth may be easily destroyed but a further growth is found in the bladder in a few months or a year's time. This can be destroyed and after a variable interval another tumour is found, which can also be destroyed. The patient may go on for many years, or for the rest of his life, forming an occasional recurrent growth which can always be destroyed.

(3) In this group, there are usually multiple growths present when first seen and whilst these have the cystoscopic and histological criteria of being benign, and appear to shrivel quite easily with the diathermy electrode, at each subsequent cystoscopic examination multiple papillomata are found. In this group, at the end of a varying time—5 or 10 years or longer—a growth appears which does not respond to cystoscopic diathermy, histologically it is malignant and more radical treatment is necessary to destroy it.

Malignant

In these tumours there is a wide variation in the histological picture. Several classifications have been suggested but that of Dukes and Masina is satisfactory and comprehensive.

(1) Papillary transitional cell carcinoma
(2) Solid transitional cell carcinoma.
(3) Transitional cell carcinoma with metaplasia.
(4) Squamous cell carcinoma.
(5) Adeno-carcinoma
(6) Anaplastic spheroidal cell carcinoma

The majority of malignant growths occur in the first three groups.

Besides seeing the type of growth, some grading is possible histologically, and three grades are generally employed; low, average, and high malignancy. The macroscopic appearance of malignant growths varies. The low grade malignant transitional cell papilloma may be difficult to distinguish from the benign tumour, but is suggested when the fronds are short, irregular, fleshy and broad, and have ulcerated or become encrusted with phosphates. Œdema around the base of the tumour is also suggestive of malignancy. The solid growths are not difficult to distinguish. They are entirely irregular, quite sessile, may be smooth and bald, but more often are nobbly, red, angry, and ugly looking. There is one type which gives rise to great difficulty in diagnosis—a submucous carcinoma with several areas separated from each other which often looks like an inflammatory lesion. The true nature is revealed by biopsy.

Spread of Carcinoma. Without treatment, spread of a malignant growth is inevitable. It starts in the mucous membrane and spreads circumferentially and into the cavity of the bladder but soon also grows into the bladder muscle and through it to reach the

paravesical tissues. Local lymph glands become affected, and from here the spread is to the iliac and para-aortic lymph glands. Blood-borne metastases occur in the liver, lungs, and bones. It is of considerable advantage in assessing the best method of treatment in a particular case to place it in one of the four stages (1) mucosa, (2) muscular, (3) perivesical and mobile, and (4) perivesical and fixed.

Symptoms and Signs of Epithelial Growths. In the large majority of cases the first sign is *hæmaturia* which is painless and may be profuse. Usually the blood is completely mixed with the urine, but may be more marked at the beginning or the end of the act. The first attack may last for a few hours or a few days, but almost invariably clears up with or without treatment. Very occasionally, it is so profuse as to produce exsanguination or clot retention. Exceptionally, frequency without hæmaturia may result from a papilloma arising on the trigone of the bladder.

If untreated, a benign papilloma increases in size, often quite slowly, and usually further tumours arise on other parts of the bladder. Inevitably further fronds are broken and bleeding occurs, but a patient may continue like this for years, passing blood and pieces of growth at times, but otherwise remaining comfortable and free from symptoms, until an attack of acute retention from clot or growth forces him to seek advice. He may be fortunate in his procrastination and the tumour or tumours may still be benign, but secondary growths may be malignant.

A malignant growth will also grow. It soon causes increased frequency of micturition. This may be from the space it occupies, but more often is from infiltration of the bladder wall resulting in diminished capacity, or because of secondary infection. Pain also occurs and is usually due to extension outside the bladder. Some advanced cases remain surprisingly comfortable but the majority are in great distress. There is severe strangury from the constant attempt of the bladder to empty itself. There may be associated difficulty in micturition and this is always so if the growth involves the internal meatus. Secondary deposits in bone give rise to aching and lancinating pain and it may be that direct spread occurs into the pelvis and a hip joint, making walking impossible and movement intolerable on account of excruciating pain.

Diagnosis and Assessment of Malignancy. This depends on four main examinations:

(1) Cystoscopy. The diagnosis of a bladder growth is made by cystoscopy and it is usually quite obvious. A small neoplasm on the anterior wall near the internal meatus may be overlooked and the examination should be made with the patient on a urological table, or in the lithotomy position With the viewing end of the cystoscope well depressed it should always be possible to obtain a view of this area. If bleeding is very severe the visibility is masked, and clots may completely obscure the view. An irrigating instrument usually overcomes the first difficulty and clots should be evacuated, but if the view is still unsatisfactory, a further cystoscopy should be done in a few days, when the bleeding will have stopped or at any rate lessened sufficiently. Much information can be gained from the cystoscopic examination and the details of this should be charted on a suitable bladder diagram The position, and extent of the growth is noted and whether it has the benign or malignant characteristics detailed above. If more than one is present, each should be indicated.

(2) Bimanual Examination. Except in the very thin and co-operative patient, this should be done under full anæsthesia with the bladder empty. A benign pedunculated tumour cannot be felt unless it is quite big and the patient is thin. Then it will be soft, and

may be felt to slip about in the inside of the bladder. An infiltrating neoplasm (Masina and Dukes—Stage 2, 3, and 4) can always be felt on careful bi-manual examination. A note must be made as to its size, consistency, and mobility in relation to the surrounding tissues.

(3) X-RAY EXAMINATION. An intravenous pyelogram should be done in all cases of bladder growth. In the apparently benign case, the upper urinary tract should be normal.



FIG 38 Filling defect in cystogram from pedunculated villous papilloma.

There should be no dilatation or stasis in the ureter on the side of the lesion and whilst there may be a small filling defect, this should be in the bladder cavity shadow and not involving the wall (*see* Fig. 38).

In a malignant growth the upper urinary tract may be normal, but if there is a hydronephrosis or hydro-ureter on the side of the lesion, and if this is known to obscure the ureteric orifice on cystoscopy, the diagnosis is confirmed since the growth has probably infiltrated the wall of the ureter. In the early stages of infiltration, there may be a little indentation of the bladder circumferential shadow (*see* Fig. 39 (*a*)), but in Stage 2 onwards, there is a well marked "bite" deformity which is quite characteristic. Occasionally, an opaque deposit may be seen on a growth on plain X-ray. In such a case, in the absence of previous diathermy treatment, the tumour is invariably malignant.

(4) BIOPSY OF THE GROWTH. If a growth is small and has all the appearances of being benign, it may then and there be destroyed with a diathermy electrode. If, on the other hand, its malignancy is doubtful, a biopsy should be taken. It may be important also in deciding the best line of treatment, to know the histology in an obvious carcinoma.

(a)

(b)



Fig 39 (a) The filling defect seen on cystogram when there is a large occupying the bladder cavity. This is not (b) T in such a case.

A biopsy is taken with cystoscopic forceps, such as that designed by Lowsley, or if near the internal meatus, it may be easier to use the McCarthy resectoscope.

Treatment of Epithelial Tumours of the Bladder. This will vary considerably with the degree of malignancy, the histological type of tumour, the size, position and the stage of the growth, the age and physical condition of the patient, and the facilities and skill of the surgeon.

Diathermy

(1) Cysto-diathermy. This is applicable to all benign growths, for malignant growths of Stage 1 and probably for malignant growths of Stage 2. The growth can be destroyed by diathermy either endoscopically or after the bladder has been opened. The choice of approach will depend on the size and position of the growth in relation to the instruments available and the skill of the surgeon.

(*a*) Endoscopic Diathermy. This is the best method of treatment from the patient's point of view and should always be employed if the surgeon thinks he can destroy the growth in one or two treatments.

Method. Two instruments are in common use for this both designed by McCarthy. The pan-endoscope and the resectoscope. With the latter, quite an extensive growth can be quickly resected. This instrument is especially useful when the growth is situated near the internal meatus, but it can also be employed elsewhere in the bladder, and the base of the neoplasm together with normal bladder muscle can be removed under direct vision. If the instrument is used blindly, the method is not free from danger and bleeding from a hidden vessel may occur, which is difficult to stop. Irrigation and a right angled telescope with a wide field, are helpful in this situation. After the main part of the neoplasm has been removed, its base may be coagulated through the same instrument. An advantage of the resectoscope is that the fragments removed by means of it are suitable for an accurate histological examination.

The second instrument extensively employed is the Pan-endoscope and is especially suitable for smaller growths or seedlings. Different sized sheaths up to 28 Charrière size, are available and through this a quite large, rigid ball-electrode can be passed. This can be accurately directed at the surface of the neoplasm which is methodically and quite quickly destroyed. The rigid electrode has a great advantage over the flexible instrument which must be employed with the older models of operating cystoscopes. Such an instrument still has some place however, as small recurrences can be dealt with quite expeditiously through it and if a recurrence is on the anterior wall a flexible electrode is especially useful. In employing diathermy, it is essential that the instruments are fool proof and that the staff are completely conversant with the correct use of the machine as a whole The operator must be familiar with the necessary strength of current which will vary directly with the size of the electrode in use.

(*b*) Transvesical Diathermy. This is employed for a benign growth or a malignant growth of Stage 1 too large to be destroyed in two treatments employing endoscopic diathermy It is especially useful for the large single pedunculated papilloma over 5 cm. in diameter and may also be employed in multiple papillomata especially when these are round the bladder neck on the anterior aspect and not easily accessible endoscopically.

Method. A careful cystoscopic examination is made with an irrigating cystoscope,

of treatment is due really to bad selection of cases. Irradiation may be applied by implantation of radium or radio-active material into the growth. It may be a surface application emanating from a radio-active substance in the bladder cavity or the radiation may be given from without by means of high-voltage X-ray or radio-active cobalt.

Implantation Irradiation. The oldest forms of this are the employment of interstitial radium and radon seeds. These may be introduced in several ways. Radon seeds have been inserted into the substance of a tumour through the pan endoscope, with a special introducer. This is not a satisfactory method as the site of introduction may be quite inaccurate. With the bladder open, the growth may be resected with diathermy down to its base and radium needles, radon seeds, radio-active gold seeds, or tantallum wire may be introduced under direct vision with planned accuracy. Radon and activated gold seeds remain in the bladder, which is an advantage as the organ can be closed. The radium needles must later be removed and so the bladder must be kept open. Tantallum wire introduced by means of a special needle (Wallace) can be attached to a catheter and subsequently brought out along the urethra. All these methods are suitable for a growth in any position. If the growth is accessible, radium needles can be passed into its base extravesically with accuracy and the bladder can be closed and usually remains so (Ogier Ward).

Intra Cavity Irradiation. This has been applied by introducing radioactive isotopes in large Foley catheter type bags. It may help in the case of multiple papillomatosis or in widespread sub-mucous carcinoma. On the whole it has not been very satisfactory. The depth of penetration of emanation is limited to 0·3 cm. and it is doubtful if the results are as good as can be obtained by careful endoscopic diathermy. Recently, Higham has applied the intra-cavity method by arranging radium needles in special rubber applicators designed to treat the surface of the growth.

X-Ray Irradiation. It is doubtful if low powered X-ray therapy machines do as much good as harm in the treatment of bladder growths. Certain of the newer machines however, are providing more hopeful results and it may well be that this treatment should be tried on early cases and not as in the past reserved mainly for those of Stage 4. A rapidly growing carcinoma often responds well whereas a well-differentiated squamous cell growth is rarely altered

Mesothelial Tumours

As with those of the kidney, mesothelial tumours can occur at any age, but are much more common in early childhood than in later years. Rhabdomyosarcoma is the most important bladder tumour in children. It is far from common and though it spreads fairly rapidly, distant metastases are late in their appearance. The tumour seems to start in the trigone or near the bladder outlet and the naked-eye appearance has been likened *to a bunch of white grapes The polypoid, gelatinous masses are very loosely joined to* each other and easily separate on manipulation. The tumour gives rise to obstruction and infection quite early on. A somewhat similar tumour is found in the adult, although it is quite rare. It is then more fleshy in appearance and appears to be enucleable. This may be only apparent for whilst part of the tumour can be shelled out, the base of the bladder may be indurated and adherent to the side wall of the pelvis. Histologically, these tumours are mixed and whilst the cellular contents may be scanty, striated muscle

fibres are usually present. Occasionally lymphosarcoma and reticulo endothelial tumours are encountered.

Signs and Symptoms. In the child the symptoms are those of a lower urinary infection with frequency and dysuria. According to Twistington Higgins, Williams, and Nash, severe spasmodic pain is a fairly characteristic feature. Transient hæmaturia is often present. In most cases, when first seen the bladder is found to be distended and there is already back pressure on the upper urinary tract. On catheterization only a small amount of urine is withdrawn. The bladder tumour is not appreciably diminished, and is now found to be more solid. A cystogram may suggest the diagnosis if an irregular filling defect, as from multiple cysts, is seen at the base of the bladder. In the adult, the condition is usually discovered as the result of investigation of either a bladder tumour or of lower urinary obstruction. On cystoscopy, the tumour is solid, fleshy, and pedunculated and this appearance together with the history, suggests that the histology may be somewhat unusual and a biopsy should be done.

Treatment. In children, the tumour is insensitive to X-rays, and total cystectomy appears to be the treatment of choice. In adults, the condition is usually too far advanced to be able to influence its course. In the low grade malignancy group, the tumour can be shelled out like a fibroid but it is doubtful if this provides more than a temporary relief to obstruction. Lympho-sarcoma can be controlled by irradiation.

Calculus Disease

Up to the present century the field for the surgical treatment of calculus disease of the urinary tract was largely confined to the bladder. Prior to the introduction of X-rays, diagnosis was inaccurate and often impossible so that kidney stones were not often treated surgically, but furthermore, stone in the bladder was far more common than it is today and occurred in the younger age groups of the population and especially in childhood. In this country and in America, calculus disease of the bladder as a primary disease is now rare, and is nearly always secondary to some other lesion. In other parts of the world, it is still quite common however, e.g. in certain Indian provinces, in China, and in South America and in these regions it is thought that its incidence is dietetic and is most likely due to a deficiency. This may be a vitamin deficiency or may be a low protein carbohydrate ratio. Curiously enough in Africa where climatic and dietetic conditions seem to be similar to those in the "stone" areas in other regions, its occurrence is rare.

Pathology. The commonest cause of bladder stone is a lower urinary obstruction. This may be due to simple enlargement of the prostate, to a muscle or fibrous bar bladder neck, or to stricture of the urethra. Stones may form from any of the constituents of the urine and the composition in any particular case, may be influenced by the reaction of the urine or by infection. The common primary stone is composed of phosphates. It may be single when it is usually fairly large, greyish white in colour, and a little rough and irregular. Multiple phosphatic stones are quite common and are then white and markedly faceted. If the urine is infected, the surface of the stone becomes covered with inspissated muco-pus which is layed down in layers together with some phosphates on the hardened surface. If a large single stone is cut across its life history becomes evident when the layers which have formed round a central core can be easily distinguished. Calcium oxalate stones assume the most bizarre shapes, some may be spiked like a hedgehog or roughened like a mulberry and both these are quite common forms. In others, the stone

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suprapubic lithotomy or by litholapaxy. In the latter the stone is crushed with a lithotrite and the fragments are evacuated by means of a suction pump such as a Bigelow's evacuator. Modern lithotrites carry a telescope and illumination but it is doubtful if this compensates for the necessary increase in size in the instrument. Litholapaxy is contraindicated if there is a neoplasm of the bladder or an enlarged prostate. If a sacculation is present, it may be burst by the high pressure of the evacuator during the removal of the crushed fragments. It may not be possible to pass a lithotrite of suitable size or indeed one at all, if there is a stricture or other narrowing of the urethra. The stone is unsuitable for crushing if it is too large, too small, too hard, too soft, or if there are too many present at one time.

Foreign Bodies

A foreign body may reach the bladder through one of various routes. The commonest of course, is along the urethra, but it may have been introduced along a suprapubic fistula, may pass in as the result of injury or following operation, or may reach the bladder by way of the alimentary tract.

(1) Through the Urethra. (*a*) *By the patient.* Many and bizarre are the objects which have been found in the bladder; indeed it is difficult to think of a small elongated object which has not been recovered from this unusual resting place. Most of these articles have been passed by the patient and whilst in some cases this has been done accidentally or out of curiosity, in most instances the object has slipped in inadvertently whilst it was being employed as a means of producing an orifice eroticism. Such objects as hairpins, safety pins, paper and hair clips are quite common, thin tubing, of rubber or plastic material, and a leather bootlace have been described, and chewing gum and wax have also been found. Perhaps the most bizarre in the literature are three caudal vertebræ of a squirrel, and 18 cm. of a decapitated grass snake. Amongst the accidental introductions may be instanced, a piece of slippery elm bark and a thermometer, the one having been used in an attempt to produce an abortion, and the other in trying to take the pelvic temperature in order to find the ovulation period.

(*b*) *By the surgeon.* If a faulty instrument has been passed along the urethra, part of it may break off and be retained. A filiform guide has remained in the bladder as has the tip of a ureteric catheter, and especially one made of plastic material which has been passed through a cystoscope. If a catheter is left draining the bladder for a long time, the tip may become encrusted with phosphates and then sometimes breaks off. This is especially likely if the instrument is of the de Pezzer or Malecôt self-retaining type. A glass catheter at one time was commonly employed in catheterizing a female and has been known to have broken and fragments remain in the bladder.

(2) Through a Suprapubic Fistula. The end of a tube occasionally breaks off and remains in the bladder. If a patient is mentally disturbed, suitably shaped articles such as a match stick may be introduced

(3) After Injury or Operation. A piece of bone has been found in the bladder following a fractured pelvis with rupture of the bladder wall. Very occasionally part of a missile comes to rest in the bladder and such has been voided along the urethra. If unabsorbable suture material is used in stitching the bladder, a stone is likely to form around it and it will remain a source of trouble until it is removed. Such stone formation has also happened around chromic catgut in the presence of infection. Foreign bodies

has the appearance of a piece of quartz or barley sugar. These shapes are due to crystallization and such a stone only occurs when there is residual urine. Uric acid stones are commoner in the bladder than elsewhere in the urinary tract. They are rounded and smooth usually multiple, and may have bosselated marks on them. Some uric acid stones are very similar to small flattened pebbles found at the seaside. They may have a layer of phosphate deposited on them and will then give a ring appearance on X-ray.

Cystine stones are much less commonly found in the bladder than in the kidney. They usually form in the latter organ and when passed from it are usually voided spontaneously along the urethra.

Apart from the curious shapes arising from crystallization, and the faceted multiple types, a stone which forms in a small diverticulum may develop a bladder extension and they become dumb-bell shaped. Similarly a stone forming in a prostatic fossa after enucleation of the gland may grow into the bladder and have a similar sort of shape to the fossa. A malignant growth of the bladder sometimes develops a phosphatic encrustation and this is especially seen with a growth in a diverticulum. The encrustation may become quite dense and hard and become an attached calculus. Phosphatic encrustation also occasionally develops after a growth has been destroyed with diathermy. A small area of encrustation is seen on the bladder wall and the surrounding area is often a little reddened and œdematous. This occasionally, but by no means always, indicates that the growth is malignant. Stone is quite often associated with Bilharzia of the bladder and any foreign body which has been introduced into the bladder may form the nucleus of a calculus.

Signs and Symptoms. Stone, secondary to an obstructive lesion, does not often give rise to symptoms. Cushioned as it is with residual urine, it is only when it becomes impacted at the internal urinary meatus that symptoms occur. In this situation the most striking complaint is difficulty in micturition which may go on to complete retention, but pain is also usually quite common. The presence of stone is discovered on investigation of the case; by X-ray in the case of all stones, other than those composed of pure uric acid, the latter are not opaque to X-rays but can be seen on cystoscopy. The rather unusual X-ray appearance of an encrusted neoplasm should suggest the underlying pathological condition. Primary stone of the bladder gives rise to some of the symptoms experienced in cystitis. There is pain at the end of micturition with a desire to pass remaining after the bladder has been emptied until sufficient urine comes down from the kidneys to cushion the stone. As well as pain, there may be difficulty in starting the act of micturition and a stopping and starting stream is often experienced.

The *Diagnosis* of Vesical Calculus is established by X-ray or cystoscopy or a combination of the two in nearly every instance.

Treatment. The removal of a secondary stone or stones from the bladder is usually an incident in the operative treatment of the primary condition. If the bladder has to be opened, the stone is removed with suitable forceps; unless the stone is very big this can be done through the bladder neck if a retropubic or perineal prostatectomy has been performed If there are multiple stones it is important that the number should be ascertained and that they should all be accounted for before considering the bladder clear. The presence of a stone complicating an obstruction or neoplastic condition may influence the operative approach and encourage the surgeon to open the bladder instead of employing the transurethral route. Primary stone of the bladder may be treated by

suprapubic lithotomy or by litholapaxy. In the latter the stone is crushed with a lithotrite and the fragments are evacuated by means of a suction pump such as a Bigelow's evacuator. Modern lithotrites carry a telescope and illumination but it is doubtful if this compensates for the necessary increase in size in the instrument. Litholapaxy is contraindicated if there is a neoplasm of the bladder or an enlarged prostate. If a sacculation is present, it may be burst by the high pressure of the evacuator during the removal of the crushed fragments. It may not be possible to pass a lithotrite of suitable size or indeed one at all, if there is a stricture or other narrowing of the urethra. The stone is unsuitable for crushing if it is too large, too small, too hard, too soft, or if there are too many present at one time.

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prostate, muscle bar obstruction, and Marion's Disease. There are at least two distinct conditions which differ in ætiology and in their clinical course:

(*a*) Congenital muscle bar obstruction and (*b*) Acquired fibrous bar obstruction.

(*a*) Congenital Muscle Bar Obstruction

In 1927 Marion described the syndrome of difficulty in micturition, residual urine, and one or more larger diverticula of the bladder occurring in young or comparatively young males. This is a definite clinical entity. It is a common cause of lower urinary obstruction in young children, especially boys, and the more severe the obstruction, the earlier does the patient present for treatment. Because of the age group, because it occurs in infancy, and because of the length of history when seen in adults, it is almost certain that the condition has a congenital origin. The bladder neck is hypertrophied but this is not always easy to demonstrate cystoscopically. It has been suggested that the hypertrophy can be distinguished by feeling it with a finger in the rectum against an instrument in the prostatic urethra. I am unable to do this. The bladder muscle is often, but not always, trabeculated but there is nearly always a diverticulum of the bladder present. This, at first, takes up all back pressure and acts as a safety valve but later may not compensate completely for the obstruction and back pressure effects may be seen in the ureters and kidneys. Section of this hypertrophied ring at the neck of the bladder, in the large majority of cases, shows that it is composed entirely of muscle. In the older age groups, there may also be some prostatic tissue Infection of the urine is uncommon and in its absence there is no histological evidence of fibrosis in this bar. The prostate in such a case, may of course be fibrous but it is not the obstructing factor, as can easily be demonstrated on cysto-urethroscopy, when the prostatic urethra opens up, as it is entered, making the hypertrophied bladder neck appear almost like a diaphragm. The amount of residual urine may be very high—2–5 litres being not uncommon. Much of this of course, is contained in the diverticulum or diverticula, but in certain cases it is entirely a bladder distension when the bladder muscle may be enormously hypertrophied.

Signs and Symptoms. Because the diverticulum which is so frequently present, acts as a safety valve, the symptoms in the absence of complications are usually comparatively slight. Some difficulty in starting micturition is common and is always of long standing. The stream is poor, but the amount passed at a time may be quite average and whilst there is sometimes increased frequency of micturition, this is not by any means constant. There may however, be enuresis especially during the night. If infection occurs, and this may follow an instrumentation, the patient may become acutely ill with marked frequency and toxic manifestations. Rarely, there is chronic infection and a long history of urinary disorder with symptoms of renal inefficiency. On examination, the bladder may be palpable above the symphysis pubis; it is not tender nor is it usually very tense. Recta examination may be made difficult by the distension of the bladder or diverticulum which can sometimes be felt, but the prostatic bed is always quite flat and smooth, and there is no suggestion of any enlargement. The diagnosis is made on investigation and by elimination. The demonstration of a diverticulum, the absence of any obvious obstructing factor and the exclusion of a neurological disorder makes congenital muscle bar obstruction the most likely and only to be disproved if there is no improvement on removal of this obstruction.

such as packs, swabs, and drainage tubes which have been left following operation on the bladder and prostate, usually give rise to disturbance of micturition with pain and frequency quite early on in the post-operative period, and on cystoscopy are seen and removed, but if a swab or instrument has been left in the peritoneal cavity and finds its way to the pelvis, it may be months or even years before it gives rise to symptoms. Commonly such objects present in the rectum but may ulcerate into the bladder and provide much difficulty in diagnosis. When such an object ulcerates through the bladder wall, it produces redness and œdema often with much bullous formation which may closely resemble a neoplasm endoscopically and bimanually. It may only be after repeated biopsy that the diagnosis is suggested or becomes established.

(4) Through the Alimentary Tract. If there is an entero-vesical fistula, the contents of the bowel may pass into the bladder and vice versa, but even in the absence of a channel of communication, pins and needles have been removed from the bladder after apparently having been swallowed.

Signs and Symptoms. When a foreign body has been introduced along the urethra, the patient soon has all the symptoms of acute cystitis with marked frequency of micturition, pain at the end of the act, and probably terminal hæmaturia. The wise patient seeks medical advice early and tells an accurate story. The unwise may go for weeks or even months before consulting a doctor, often give no help in establishing the diagnosis, and may deny all knowledge of how a foreign body could have entered the bladder, even when confronted with the article. If the presence of a foreign body is suspected in the bladder, an X-ray should be taken of the bladder region and a cystoscopy performed. In most cases it is then apparent but it may be that it will only be discovered after a bladder calculus is sectioned and a foreign body is found to form its central core.

Treatment. This will depend on the shape and size of the article, on its composition and on whether or not a stone has already formed around the whole or part of it. If at all possible, it should be removed per urethra by grasping it in alligator forceps which have been passed down to the bladder through the pan-endoscope. If the foreign body is composed of wax, it may be dissolved in petrol and liquid paraffin. Otherwise, the bladder is opened suprapubically and the article lifted out with forceps.

Bar Obstruction at the Bladder Neck

There are certain fairly obvious pathological processes which produce difficulty in micturition and lead to obstruction of the lower urinary tract. Amongst these are a neoplasm at the base of the bladder which may be sessile and malignant, or pedunculated when it may be benign simple enlargement, carcinoma and calculus disease of the prostate, and obstruction in the lumen of the urethra There remains however, a very definite group of patients chiefly male, but occasionally female, in whom there is difficulty in micturition with varying amounts of residual urine. There is usually some obvious effect of obstruction, such as a diverticulum of the bladder, bilateral hydro-ureter, or a large toneless bladder which may contain several litres of residual urine. In this group of cases, there is an obstructive factor at the bladder neck, but this is difficult to demonstrate and may only be proved to have been present when there is considerable or complete relief after the continuity of the bladder neck is destroyed by the removal of part of it. This condition has been known for many years. Guthrie described it in 1832, Mercier (1837) noted it, and the condition has been called Mercier's bar, "Prostatism sans prostate," fibrous

prostate, muscle bar obstruction, and Marion's Disease. There are at least two distinct conditions which differ in ætiology and in their clinical course:

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(b) Acquired Obstruction at the Bladder Neck

This is due to fibrosis from long continued infection. It is seen in association with stricture of the urethra treated by intermittent dilatation, prostatitis, and calculus disease of the prostate. It may only be distinguished from minor degrees of middle lobe enlargement of the prostate on biopsy. The clinical effects of this form of obstruction are not the same as those found in the muscle bar. It is exceptional to find a large amount of residual urine although up to half a litre may occur. Diverticulum of the bladder is not very common and when it does occur is small, often multiple, and more like that found with simple enlargement of the prostate. The bladder wall is markedly trabeculated and sacculations are always multiple. There is usually infection in the bladder.

Signs and Symptoms. These are always much more marked than in the uncomplicated muscle bar obstruction. There is considerable difficulty in micturition together with increased frequency both day and night. In the more severe cases, the patient spends much of his time trying to pass and passing urine.

Treatment. The obstruction must be relieved. When a diverticulum is of such size that it will not drain, then it must be removed at open operation. In such a case, a wedge should be removed from the bladder neck with a diathermy knife. If, on the other hand, it is not necessary to open the bladder, the obstruction should be removed endoscopically with the resectoscope or cold punch.

Diverticulum of the Bladder

A diverticulum of the bladder has been described as arising from three causes: (i) Congenital, (ii) Traction, and (iii) Obstruction.

Congenital diverticula are wide open, occur at the fundus of the bladder, are sometimes called urachal and are of no clinical importance. Traction diverticula are also rare, occur in association with hernia and more often after this has been repaired. The diverticulum commonly met with is always associated with obstruction and is really a herniation of the mucous membrane through the muscle fibres of the bladder wall. The lining is directly continuous with the mucous membrane of the bladder cavity, and the outer wall of the diverticulum is fibrous being a condensation of peri-vesical fascia. The opening of the diverticulum is commonly in the region of a ureteric orifice either medial or lateral to it and above the trigone. The sac usually lies in the para-vesical space between the bladder and the lateral wall of the pelvis. Occasionally, the diverticulum forms on the posterior wall of the bladder rather higher up and may then present on the peritoneal surface There is often more than one sac, and then it is usual to find one on each side of the bladder, but they may both be on the same side and two distinct sacs may join together at their neck and open into the bladder through one orifice. The ureter and also the vas deferens are sometimes intimately connected with the wall of the diverticulum and lying in its adventitious fibrous layer may be damaged during removal of the sac. Rarely, the ureter opens directly into a diverticulum.

Small diverticula 0·5–2 cm in diameter, are quite common in association with simple *enlargement of the prostate, stricture of the urethra, and acquired bladder neck obstruction.* More commonly these are incompletely herniated and there is still some muscle in the wall of the sac. In such cases there may be quite a number of diverticula. The larger diverticulum is also occasionally found in association with the enlarged prostate, but much more often in the muscle bar obstruction of congenital origin.

(a)



(b)



Fig 40 (a) A diverticulum of the bladder with a filling defect due to a carcinoma (b) The specimen.

Signs and Symptoms. A diverticulum does not give rise to any symptoms and is discovered in the course of investigation. Indeed, it may act as a safety valve to lower urinary obstruction and mask this condition for many years. Should however, some other complication of the obstruction occur, then the presence of the diverticulum may well alter the whole clinical course of the case. It may be outlined in the cystogram of an intravenous pyelogram and its orifice will be seen on cystoscopy. If the sac is small, the whole thing may be seen as a shallow depression or outlet in the bladder wall but if large and the normal amount of lotion (200 c.c.–8 oz.) is being employed, the opening will appear as a crenated dark hole.

The Significance of a Diverticulum. As has been said, it acts as a safety valve. In the absence of infection it is exceptional to find renal back pressure and a raised blood urea, when one is present. It is however, a potential danger. It does not completely empty, and if infection occurs in the bladder this may give rise to a virulent cystitis and grave toxic absorption. Because of stasis, stones may form in the sac and cushioned by the fluid may grow large and may multiply. A neoplasm may form in the diverticulum and this is very often a carcinoma (*see* Fig. 40 (*a*), (*b*)). It may grow to a considerable size without giving rise to symptoms. It will spread through the wall of the sac more quickly than it would through the bladder wall and the prognosis is nearly always more grave than in vesical neoplasm. This is probably not so when it occurs in a diverticulum which presents on the peritoneal covered part of the bladder. The diagnosis may remain in doubt until open operation, but should be suggested when there is hæmaturia and a typical orifice is seen on cystoscopy, or when a palpable lesion is felt on bimanual examination, and very little can be seen in the bladder at cystoscopy. There is always an obstruction as well as the diverticulum. If the latter alone is removed, one of three things will happen: (1) The most likely is that the opening in the bladder will break down and a persistent fistula will form. If the bladder wound heals, then either (2) another diverticulum will form or (3) bilateral hydro-ureter will develop. Should the obstruction be removed and the diverticulum still remain, there will be persistent infection and perhaps recurring stone formation after an endoscopic operation, or a suprapubic fistula will persist if the bladder has been opened.

Treatment. The diverticulum is removed at open operation. Excision of a wedge from the orifice with a resectoscope or punch cannot allow complete emptying, either theoretically or in practice, but when open operation is strongly contra-indicated such a procedure may help drainage. The diverticulum can be removed through the bladder, extra-vesically or by a combination of these approaches and with a large sac this is nearly always advisable. If small, it may be invaginated into the bladder and removed either through the opened bladder, or, if a retropubic prostatectomy has been done, through the bladder neck. The bladder need not be drained suprapubically, but the para-vesical space should always be drained for at least 4 days.

NEUROLOGICAL AND PHYSIOLOGICAL DISORDERS OF MICTURITION

Anatomical Considerations

The nerve supply of the bladder comes from each pelvic plexus which in turn is enervated by branches from sacral and lumbar roots. The sacral, which is the more important, comes from 2, 3, and 4 segments and carries both motor and sensory fibres.

The lumbar supply from 2, 3, and 4 segments passes by way of the pre-sacral or hypogastric nerves and mainly supplies the internal genital organs.

The Act of Micturition. Micturition is the reflex response to stretching of the muscle fibres of the bladder wall and depends on the integrity of certain pathways. There is a spinal reflex arc with its centre in the sacral segment of the cord, but the action of the reflex can be prevented by inhibiting impulses from the cortex which act on the central synapses of the reflex arc. The exact pathway of these impulses has not yet been accurately determined. Voluntary micturition is therefore a release of inhibition, but the act is more than a simple spinal reflex since the bladder does not completely empty when the cord has been transected even though the reflex arc remains intact. It may be that, after transection, the external sphincter which is under voluntary control, acts independently and without co-ordination with this reflex.

Neurological Disorders

Disorder of micturition always occurs where there is complete trans-section of the cord; it frequently occurs in certain nervous diseases such as tabes dorsalis and disseminated sclerosis and is occasionally noted in others such as poliomyelitis and subacute combined degeneration of the cord. Micturition may be upset after an extensive pelvic operation such as abdomino-perineal excision of the lower bowel and Wertheim's radical hysterectomy. This upset may be temporary or permanent depending on whether it is due to a partial or complete lesion of the pelvic plexus. If the nerve injury has been in the nature of a contusion, recovery may be expected but it can take up to six months for this to occur.

Acute Retention

This follows injury to the cord but may also result from a sudden hæmorrhage into a tumour. In the latter case, there may have been premonitory urinary symptoms such as increased frequency or a little difficulty in starting. Acute retention has also been seen at the onset of poliomyelitis and indeed has been the presenting symptom. Fracture dislocation of the spine is the commonest traumatic cause, and in this case the effect is usually complete and permanent from the beginning. In gun shot wounds involving the spine, the lesion is often partial from the beginning and even when at first complete some recovery is not infrequent.

Symptoms and Signs. There are two principal stages—Atony and Hypertonicity.

(1) Stage of Atony. Immediately after transection of the cord, the bladder becomes completely atonic and a painless soft distension occurs. If this is not relieved a dribbling overflow occurs in some 48 hours and at this stage some blood may be found in the urine from over-stretching of the bladder wall. If the patient survives, after a period which is rather variable, but usually some 6–8 weeks, the second stage occurs.

(2) Stage of Hypertonicity. The bladder muscle develops a tone which is considerably increased over normal and the capacity of the organ is diminished. In spite of strong contractions of the bladder muscle, emptying is inadequate, residual urine is considerable and may be almost as much as the total bladder capacity. There is therefore almost constant involuntary dribbling If the lesion in the cord is at the sacral level or affects it, no further recovery in function takes place. If however, the lesion is higher in the cord and the reflex arc remains intact, considerable improvement in emptying will occur and

the so-called automatic or cord bladder develops. In this case, the bladder fills fairly well and the period between evacuations lengthens and may ultimately be several hours. The patient has no voluntary control over the act but is dry in between times and may be able to gauge the time of emptying with some accuracy. In some cases he may develop a "trigger" mechanism which will precipitate voiding. This differs with the individual but pinching the glans penis, stroking the perineum or inside of the thigh, and maximal pressure on the suprapubic region have each on occasion initiated evacuation of the bladder.

Treatment. In the early stages, the bladder must be emptied. Opinion is by no means unanimous as to the best way of affecting this. Except when it works with very little effort, manual compression of the bladder should be avoided. In special centres, there is much to be said for intermittent catheterization, especially during the first 2–3 weeks when trophic changes may occur in the urethra. There is still a considerable opinion in favour of drainage and no unanimity as to whether this should be by an indwelling catheter or by a suprapubic tube. There would appear to be little difference in the end results provided each is done with care, nor does there seem to be much advantage with regard to ultimate bladder function, whether tidal drainage is used or not. It is probable that suprapubic drainage requires a little more equipment but a little less supervision than urethral drainage. A Riches' tube is very suitable for use in a paraplegic patient. It is essential that the drain should emerge at least 2 in. above the symphysis. If low, leakage occurs around the tube and it may be difficult to keep the wound dry; when the time comes to allow the bladder to close, a long oblique fistulous track closes readily. A Foley catheter is the most suitable for use in the urethra and must of course, be introduced with full surgical precautions against infection. In most instances, it is well tolerated but every now and then an acute urethritis develops and may become fulminating if the catheter is not immediately removed. In such a case, the penis swells, becomes tender and inflamed, and a peri-urethral abscess with fistulous formation may follow.

The pH of the patient's urine should be kept acid and extra fluids (3 litres daily) should be administered. A bladder irrigation with a syringe should be given once a day or oftener if necessary. This will flush the sediment which so often settles in the bas fond of the bladder and will help to diminish the formation of stone. Whilst the urological care of cases of paraplegia at this stage is of prime importance, the general treatment of the patient is also most important. He is encouraged to use every muscle he can and any activity which allows him to do this is initiated. Exercise of the upper limbs and trunk are practised and frequent changes of position help to prevent pressure sores and may also make the formation of decubitus calculi less likely.

Later Treatment. In the higher transection, within a few weeks the bladder will have become automatic and the urethral catheter or suprapubic tube is now removed. If the suprapubic fistula has been established at the right level with a long track it quite often closes and heals spontaneously. Should this not happen within 48 hours and the patient remain wet, a catheter is passed and fixed in the urethra. A Foley catheter with a 5 c.c. balloon should be tried but if this fails a Harris or Tieman's type should be tried. When the suprapubic opening has been dry for 5–6 days, the catheter may be tried out. Frequency will at first be quite marked, but in due course the interval between emptying becomes longer and in a good case may be up to 5 hours; there will of course be no control in starting or stopping the act and so a rubber urinal must be fitted. If a patient

finds, or develops, a trigger mechanism, he may be able to dispense with this urinal at certain times during the day, although if he is engaging in any muscular activity, it is wise for him to have the urinal. Even in the best case, however, the bladder is never completely emptied and urinary infection is very common. Because of this and stasis, stone formation is quite common. Flushing the tract and exercise undoubtedly help to minimize this, but a watch must be kept for its occurrence. If a calculus is suspected, X-ray and endoscopic investigation is undertaken and if found is treated in the most conservative way possible. If renal, even when the kidney function on one side may seem to indicate nephrectomy, this should be avoided if at all possible. Stone in the bladder is treated by litholopaxy.

In the closed autonomous bladder, when the spinal arc is interrupted or the sacral centre has been destroyed, the end result is not nearly so good as that detailed above. After the stage of atony the bladder muscle becomes hypertonic but is almost unable to empty the organ so that the difference between total capacity and residual urine is only a few cubic centimetres. This spurts out every few minutes and the patient is constantly wet. Sometimes abdominal muscle exercise and manual suprapubic pressure may help, but a rubber urinal must be constantly worn. The work of Emmett and Dunn (1946) showed that resection of a small amount of muscle from the neck of the bladder at the posterior commissure sometimes resulted in marked improvement. The quantity of residual urine is markedly diminished and the bladder now empties intermittently. The patient is of course still incontinent but is dry between acts of voiding.

Chronic Retention

This may be seen in spina bifida (*see* Fig. 41). It may occur in Tabes Dorsalis and Disseminated Sclerosis. It is seen in certain conditions when the cauda equina is compressed as in spondylolisthesis, and has been found in association with radiculitis in diabetes mellitus. It has also followed spinal anæsthesia.

Symptoms and Signs. There may be no urinary symptoms and an over-distended bladder may be discovered on routine physical examination. On the other hand, some frequency and often urgency is common and nocturnal enuresis may be the presenting symptom. The diagnosis of chronic retention is easy but that of the cause may be extremely difficult. The presence of the neurological disease must be established and a mechanical cause must be eliminated by rectal and endoscopic examination. It may well be that the latter will confirm the diagnosis as in neurogenic retention the bladder neck is wide open and funnel shaped and the verumontanum can be seen in the same cystoscopic field as the ureteric orifices, with an ordinary examining instrument. Trabeculation due to a mechanical obstruction is usually coarse with wide and often thick bundles, whilst in neurological dysfunction, any trabeculation is quite fine and the groups of muscle fibres slender. It is unusual for the kidney function to be upset in chronic neurological retention, unless the bladder has become infected.

Treatment. Sometimes by abdominal exercise and manual suprapubic compression, the patient can help considerably the emptying power of the bladder. Carbachol taken by mouth in doses of 2 mg. three times daily is also of use. There does not seem to be much place for bladder neck resection in the chronic retention of tabes dorsalis, although certain cases have been helped and it may be worth trying the effects of a minimal resection. In a number of cases, however, some bladder drainage must be instituted. If at all

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It is much more common amongst boys than girls and there is sometimes a familial tendency. Lack of control is much more common at night than during the day. Bed-wetting or the wetting of clothes may of course be a symptom of a serious urological disorder but in the large majority of cases after the most exhaustive investigation, no cause is found for the condition. Amongst the pathological lesions which may produce enuresis in children are:

(1) Chronic retention with overflow from lower urinary obstruction such as posterior urethral valves or a muscle bar obstruction at the bladder neck.

(2) A cauda equinal lesion from a spina bifida.

(3) Ectopic opening of a ureter—especially in the female.

(4) Chronic infection.

(5) Minor lesions such as phimosis, balanitis, and a long prepuce have been thought to cause bedwetting.

(6) Winsbury White considers tags and polyps on the posterior urethra are responsible for many cases but his observations have not been confirmed.

(7) Conditions outside the urinary tract such as anal fissure, threadworms and other intestinal parasites, vaginitis, vulvitis, infected tonsils, and adenoids have all been considered to be causes, since if these are successfully treated, the enuresis, certainly in some cases, stops.

Management of a Case. The child should be fully examined to eliminate any obvious cause of the lack of control. If the urine is crystal clear and contains no abnormality, and if it is thought the bladder empties on micturition, endoscopic urological investigation should not be undertaken at this stage. If there is a physical abnormality, it should always be corrected, since it may be the cause. If on the other hand, nothing abnormal can be found, a simple but regular regime should be instituted. The child should be encouraged to empty the bladder at fixed times and, over a period, the interval between voiding is gradually lengthened. Fluids should be restricted during a period of two hours before going to bed, and the last meal should be dry, simply consisting of cereals or bread and butter, and nothing sweet or salty should be given with it. He should not be allowed to take part in any strenuous games from the late afternoon onwards, nor should he be allowed to become over-excited either by watching or taking part in plays, dancing, etc., The child should be wakened regularly at 10 p.m. and made to empty the bladder. It will be found that with this regime quite a number of children develop normal control but a core of cases remains who continue to bedwet frequently and even nightly. In many the tendency is undoubtedly increased when the child is tired and most are found to be heavy sleepers. Treatment is directed to diminish this tendency so that the bladder filling impulses may register in the cortex and the normally inhibiting mechanism is brought into play. Remedies employed with some and often complete success are tincture of belladonna by mouth in increasing doses together with ephedrine and amphetamine sulphate. Some grow out of the habit about puberty and this is especially so in the female. With this in mind, androgens and œstrogens have been given and some improvement is claimed to have occurred after their administration.

Atony of the Bladder

In this condition the bladder contains a considerable quantity of urine—upwards of a pint—after micturition. The bladder muscle is lax, the intra vesical pressure is quite low,

possible, intermittent urethral catheterization should be employed, as a permanent suprapubic cystostomy always leaks and the patient is miserable. Transplantation of the ureters into an isolated loop of ileum may make the patient much more comfortable giving him a controlled fistula.



FIG 41. Urogram in boy of twelve with spina bifida. Note the dilated prostatic urethra (Mr. D. F. Ellison Nash's case)

Physiological Disorders

The Enuresis of Childhood

Lack of urinary control is a fairly common and distressing condition which is found amongst children in all strata of economics and intelligence. It is more prevalent in the poorer classes however, and in many cases is due to lack of, or improper training.

It is much more common amongst boys than girls and there is sometimes a familial tendency. Lack of control is much more common at night than during the day. Bed-wetting or the wetting of clothes may of course be a symptom of a serious urological disorder but in the large majority of cases after the most exhaustive investigation, no cause is found for the condition. Amongst the pathological lesions which may produce enuresis in children are:

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(3) Ectopic opening of a ureter—especially in the female.

(4) Chronic infection

(5) Minor lesions such as phimosis, balanitis, and a long prepuce have been thought to cause bedwetting.

(6) Winsbury White considers tags and polyps on the posterior urethra are responsible for many cases but his observations have not been confirmed.

(7) Conditions outside the urinary tract such as anal fissure, threadworms and other intestinal parasites, vaginitis, vulvitis, infected tonsils, and adenoids have all been considered to be causes, since if these are successfully treated, the enuresis, certainly in some cases, stops.

Management of a Case. The child should be fully examined to eliminate any obvious cause of the lack of control. If the urine is crystal clear and contains no abnormality, and if it is thought the bladder empties on micturition, endoscopic urological investigation should not be undertaken at this stage. If there is a physical abnormality, it should always be corrected, since it may be the cause. If on the other hand, nothing abnormal can be found, a simple but regular regime should be instituted. The child should be encouraged to empty the bladder at fixed times and, over a period, the interval between voiding is gradually lengthened. Fluids should be restricted during a period of two hours before going to bed, and the last meal should be dry, simply consisting of cereals or bread and butter, and nothing sweet or salty should be given with it. He should not be allowed to take part in any strenuous games from the late afternoon onwards, nor should he be allowed to become over-excited either by watching or taking part in plays, dancing, etc., The child should be wakened regularly at 10 p.m. and made to empty the bladder. It will be found that with this regime quite a number of children develop normal control but a core of cases remains who continue to bedwet frequently and even nightly. In many the tendency is undoubtedly increased when the child is tired and most are found to be heavy sleepers. Treatment is directed to diminish this tendency so that the bladder filling impulses may register in the cortex and the normally inhibiting mechanism is brought into play. Remedies employed with some and often complete success are tincture of belladonna by mouth in increasing doses together with ephedrine and amphetamine sulphate. Some grow out of the habit about puberty and this is especially so in the female. With this in mind, androgens and œstrogens have been given and some improvement is claimed to have occurred after their administration.

Atony of the Bladder

In this condition the bladder contains a considerable quantity of urine—upwards of a pint—after micturition. The bladder muscle is lax, the intra vesical pressure is quite low,

the organ cannot be felt on palpating the abdomen, and there is no demonstrable mechanical obstruction. D. I. Williams has classified bladder atony as follows:

(1) Neurogenic.
(2) Secondary to obstruction.
(3) Primary when there is no obstruction.
(4) Primary when there is also rectal atony.

(1) *Neurogenic atony* is described on p. 101.

(2) *Atony secondary* to obstruction is seen after a bladder has been over distended for a long time. The majority regain emptying power after the obstruction is removed, but in some cases even after prolonged drainage, the bladder does not empty itself.

(3) *Primary Atony.* This is also uncommon. There is no demonstrable obstruction. The bladder muscle shows little or no trabeculation and when a catheter is introduced the intra-vesical pressure is seen to be very low, the contents of the bladder trickling out without any force.

(4) Is similar to 3 except that the rectum is also affected and there is marked difficulty in emptying the bowel. These patients are usually old and there is often evidence of cerebral softening.

Symptoms and Signs. The patient may complain of a poor stream, of frequency, or the presenting symptom may be bedwetting. The distended bladder is quite soft, is not tender, and may only be definitely determined after a catheter or cystoscope has been passed. It may only be by a process of elimination that the diagnosis is made, as when some apparent obstructing factor has been removed and yet the patient is no better.

Treatment. It is usual to try resection of the neck of the bladder but of course, if the retention is relieved by this procedure, the cause is obstruction. The effect of prolonged drainage must be tried. This is best through a urethral catheter if such can be tolerated. Sometimes, removal of the top half of the bladder helps. Carbachol should be tried, and in the fourth group daily high colonic irrigation often helps to restore the tone in both viscera. Suprapubic drainage does not often help and indeed usually makes matters worse.

Incontinence of Urine

In this state, the patient is unable to retain urine and becomes wet either by day, by night, or throughout the 24 hours, and the bladder is not distended. True incontinence may be due to a nervous disorder, such as disseminated sclerosis or cerebral thrombosis, and is sometimes found in spina bifida with a meningocele. Surgical treatment is unlikely to be of any value in such cases.

Incontinence in the Male

This may occur after any form of prostatectomy, in which the external sphincter is also injured. It is rare but occurs more commonly after perineal and endoscopic resection of the prostate than in other types of operation It is more liable to occur after retropubic than transvesical prostatectomy unless care is taken to divide the urethra at the apex of the gland, rather than to tear up a length of the membraneous part. If the control is only partly weakened, it can be strengthened by sphincter exercises and by diathermy applied to the region of the sphincter with one lead incorporated in a catheter.

If the patient is completely incontinent some help may be obtained from an external reefing operation, such as advocated by Lowesly and by Millin.

The majority of severe cases require to wear a permanent appliance which is either in the form of a rubber urinal or a spring clamp applied to the penis.

Incontinence in the Female

(*a*) Partial or Stress Incontinence. Lack of urinary control is common after childbirth and many women may have slight dampness on straining, laughing, coughing or sneezing, with a full bladder, and more especially when overtired. In a number of cases, this may be sufficiently marked to give rise to much distress and the patient may be constantly damp or wet except when sitting or lying. In many cases, but not all, there is some prolapse of the pelvic floor or anterior vaginal wall and when this is corrected, urinary control becomes adequate. In some, there is no prolapse, and stress incontinence may continue after colporrhaphy. Then some further procedure is necessary and several have been devised. The commonest of these are the Aldridge sling, the Millin sling, the Shaw hammock, and the Everard Williams cystopexy.

(*b*) Complete Incontinence. Apart from neurological diseases, this may occur after an obstetrical or gynæcological injury which involves the internal urinary meatus. The condition must be differentiated from vesico-vaginal fistula, uretero-vaginal fistula, and an ectopic opening of a ureter. Attempts at repair are usually unsatisfactory and there is no appliance which can help much to keep the patient dry—a rubber bed pan, and all appliances are quite unsatisfactory in the female. If the anal sphincter is competent a uretero-colic anastamosis must be considered otherwise an ideal hoop may help.

DISEASES OF THE PROSTATE

The prostate is one of the accessory male sex glands: its secretion forms part of the ejaculate, and is thought to stimulate the sperm to move. Its main surgical importance is twofold:

(1) It encircles the first part of the urethra, and (2) In a third of all men over the age of 50 years, it enlarges. In many it then produces a disorder of micturition. The principal diseases to which it is subject are infection, calculus disease, simple senile enlargement, and carcinoma.

Prostatitis

Infection in the prostate is not uncommon and may reach the gland via the blood stream or from the prostatic urethra. Prior to the institution of specific treatment for gonorrhœa, the gonococcus was the commonest infecting organism; now the commonest infection is from the Staphylococcus, especially the Staphylococcus albus. Infection may also be due to the Bacillus coli, to the Streptococcus fæcalis, and to the Gonococcus. A Staphylococcal infection may occur in association with an infection elsewhere, such as multiple boils or a carbuncle, or it may develop in a gland which is already the site of stone formation. Any infection may be either acute or chronic.

Acute Prostatitis

Symptoms and Signs. The first symptom is usually frequency of micturition together with urgency, but quite frequently the infection is ushered in with a rigor. Soon the

the organ cannot be felt on palpating the abdomen, and there is no demonstrable mechanical obstruction. D. I. Williams has classified bladder atony as follows:

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urine contains a few threads of pus and epithelial cells, sometimes an infecting organism can be cultured but more often nothing grows. On rectal examination, the prostate is small and flat. It may be a little granular, and one or other lobe is always tender. The epididymis is a little full and may be thickened from a previous infection. One or both are frequently tender.

(b) GROUP 2. *Signs and Symptoms.* In this group there is a history of several acute attacks of malaise with pyrexia which may or may not suggest infection of part of the



FIG. 42. Calcification of the prostate.

urinary tract If the latter appears to be affected, the symptoms or signs may suggest an acute cystoprostatitis or pyelitis and on investigation Bacillus coli is found in the urine. This is then treated appropriately, quickly settles down, and the urine becomes sterile. In a few weeks or it may be months a similar incident occurs but during the interval between the attacks, the patient seems well and the urine appears to be free from infection. In other cases there are recurring incidents of infection, which attacks different anatomical structures, e.g. recurrent irido-cyclitis and recurrent infective arthritis. There are often no symptoms referable to the urinary tract but if a smear taken after a prostatic massage is examined, infection is found to be present. Sometimes the patient presents with acute epididymo-orchitis.

The exact diagnosis may remain in doubt but can be confirmed by seeing threads exuding from the prostatic ducts on urethroscopy.

Treatment. It is first necessary to establish the infecting organism and to find to which pharmaceutical preparation it may be sensitive and for this purpose a specimen of urine obtained after a prostatic massage is cultured. An appropriate course of treatment

patient feels quite ill, there is pain in the perineum and often also in the rectum; there is a constant desire to pass water, with pain during the act, often difficulty and sometimes hæmaturia. On examination, he looks ill, the temperature is raised, the urine is hazy and contains pus and organisms; on rectal examination which must be performed very gently, one or both lobes of the prostate are a little enlarged, firm, smooth, and acutely tender.

Treatment. The patient is put to bed and given copious bland fluids to drink. An alkaline diuretic is prescribed and as the commonest infections are staphylococcal and coliform, penicillin and streptomycin together are given. At the same time stilbœstrol in doses of 10 mg. 8 hourly is administered. A specimen of urine is cultured and the sensitivity of the infecting organism ascertained. Heat to the perineum sometimes relieves the pain in this situation, but a suitable analgesic should also be prescribed. If the temperature remains elevated and pain continues, a careful assessment is made of the gland by rectal examination, to see whether or not an abscess has formed.

Prostatic Abscess. This nearly always occurs as a complication of acute prostatitis.

Signs and Symptoms. The earliest manifestations are those of acute prostatitis, dysuria, pain in the perineum, and frequency. If an abscess develops, difficulty in starting micturition increases and there may be a complete acute retention. As this abscess increases in size, so the pain in the perineum increases in severity, is constant, and is difficult to control with simple analgesics. On rectal examination, the gland is acutely tender. The lobe on the side affected is larger and in the later stages feels softened and a little boggy.

Treatment. If an abscess is diagnosed, a curved incision is made in the perineum 2 cm. anterior to the anus down to the gland which is explored with sinus forceps after the manner of Hilton. When the abscess is opened, pus exudes and a small rubber drain is left in. Subsequently, the patient is treated systemically with the most appropriate antibiotic and locally by hot hip baths. If drained early, the condition clears up completely. Should acute retention occur, the patient is given an analgesic and made to sit in a hot bath. If this is ineffective, the bladder is emptied through a rubber catheter, passed very gently Even this may cause the abscess to rupture into the urethra, after which it may subside, but drainage through this route is not very satisfactory and usually leaves a chronic prostatic infection.

Chronic Prostatitis

There are two groups of cases found in association with a chronic infection of the prostate, each of which has a definite but different syndrome. Group 1 gives rise to constant local symptoms, and Group 2 to an acute exacerbation of infection, the manifestation of which may not be local.

(*a*) GROUP 1. This, more often than not, is an infection continuing from an acute episode The patient complains of vague pain in the perineum, rectum, and testis The pain often passes down the inner side of each thigh and may reach the ankles Usually there is some disturbance of micturition, which may show as a little difficulty in starting but also as increased frequency. The patient is introspective; he often has a "guilt" complex, is gloomy, and pessimistic He becomes a constant attendant at hospital or consulting room and is difficult to treat and to reassure.

Signs and Symptoms. Symptoms are usually out of all proportion to the signs. The

(*a*) Corpora Amylacea. These are small bodies about the size and colour of a turnip seed, found quite frequently and often in considerable numbers in a simple benign enlargement of the prostate. They are composed of nucleo-protein and are probably formed from inspissated prostatic secretion and desquamated epithelium. They are usually discovered on examination of the part of the gland which has been removed and are of no clinical significance.

(*b*) True Prostatic Stones. These are of two types:

(1) *Small Multiple Calculi* (*see* Fig. 42). These may be found in association with senile enlargement. They are not present in the adenomatous part but in the line of cleavage between it and the compressed false capsule. These stones either cling to the adenoma as it comes out or remain in the fossa adhering to the capsule. In the latter case they must be removed otherwise they form a nucleus for further stone formation, which may form a cast of the whole fossa.

(2) *Massive Calculi* (*see* Fig. 43). When these are present the gland is always small and fibrous; the stones are formed in its ducts and they may in time almost completely replace the gland tissue. The prostatic stones are usually composed of calcium carbonate but may contain magnesium, phosphate, and calcium oxalate. It is not known why they form. A significant number give a history of chronic or previous urinary infection but in others there is nothing to suggest a cause.

Signs and Symptoms. It is probable that the majority of prostatic calculi may lie dormant for many years. As has been said Corpora Amylacea are of no clinical significance. When small multiple calculi are found lying between the enlarged part and the compressed false capsule in senile hypertrophy, their presence is usually first noted as the result of a routine X-ray examination and they also have little clinical significance. It is much more often with the massive calculi which are found in the small gland and which may largely replace it, that symptoms often arise. These will depend on whether or not obstruction is the main disability. When infection is present, as it often is, it probably only gives rise to symptoms when there is not free drainage into the prostatic urethra and then either one or other of the clinical syndromes associated with chronic prostatitis may develop (*see* p. 105) If a stone should ulcerate into the prostatic urethra, there may be pain and frequency of micturition with perhaps a little blood at the beginning or end of micturition. Soon some difficulty is experienced and if the stone is large, complete retention may occur. On examination per rectum, the gland with corpora amylacea or multiple calculi, may not feel different from any other simple enlargement. In the case with massive calculi, the surface of the prostate is often hard and irregular and may simulate a carcinoma. Occasionally, crepitus is made out, but the diagnosis is usually determined by X-ray. There may be a posterior urethritis and if infection is severe, epididymo-orchitis may develop

Treatment. The presence of corpora amylacea or multiple stones in association with a simple enlargement of the prostate is neither an indication for operation nor does it interfere with simple enucleation of the adenomatous part of the gland. Massive calculi when symptomless, should be left alone. If obstruction occurs from a fragment ulcerating into the prostatic urethra, a catheter is passed and this usually pushes the stone into the bladder, from where it should be removed. It may be possible to slit the prostate endoscopically with a Colling's knife and "bulldoze" the stones into the bladder from where they are removed by suction either with or without crushing (Ogier Ward). If

is then instituted and during this course, a gentle prostatic massage should be given daily or at other regular intervals, and at the same time an alkaline diuretic is given with increased fluids. Any irritant such as alcohol, spices, strong coffee, etc., are forbidden. In many cases the infection will completely clear up under this regime but in others it will not and remains very intractable. Sometimes a course of rectal diathermy may provide some relief. Incision and drainage of the prostate employing a Colling's diathermy



FIG 43. Calcification of the prostate producing acute retention

knife through the pan-endoscope may next be attempted If this fails, and if the symptoms warrant it, radical prostatectomy may be advised. It is wise to keep a balance between the clinical state of the patient before and after this operation. The latter will undoubtedly relieve him of many of his symptoms. In recurrent iritis, vision may be gradually destroyed and if in such a case, the cause is an infective focus in the prostate, total prostatectomy should always be advised. Similarly in recurring pyelitis with diminishing renal function and worsening hypertension, or in recurrent arthritis of severe degree, the radical operation must be considered but it should be remembered that 90 per cent are impotent and 10 per cent incontinent after this operation.

Calculus Disease

Stone formation in the prostate is fairly common; it usually occurs after the age of 40 years and is unknown in childhood. There are two main types:

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(*b*) TRUE PROSTATIC STONES. These are of two types:

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infection is marked, it is unlikely that it can be eliminated unless the whole prostate is removed. In considering the radical operation, the possible and probable complications should be put to the patient.

Benign Enlargement of the Prostate

This condition which is also called senile enlargement, hyperplasia, and nodular or adenomatous hypertrophy, is a very common condition. According to Deming 65 per cent of men over the age of 65 years, have some degree of this condition and it is usually estimated that a third of all men over the age of 50 years will have symptoms arising from this enlargement. The cause is not properly determined and by many it is considered to be neoplastic. It seems however, that it has some association with the male climacteric In the dog, castration and the administration of œstrogen are followed by involution of the enlargement. In the human after neither of these is there any appreciable change clinically or symptomatically in senile enlargement but on histological examination of the gland there is stratification of the normal transitional epithelium and areas of squamous cell metaplasia can be seen. It has been claimed that large doses of Testosterone Propionate may cause the enlarged gland to diminish in size. At any rate, the very high incidence of simple enlargement in men over the age of 50 years, and the absence of such enlargement having occurred in any male who has been castrated in youth (Huggins) suggests that there is a hormonic influence in its development. The enlargement is nodular and may affect particular lobes of the gland. Each nodule is composed of glandular, muscular, and fibrous tissue and may reach a considerable size. The nodules compress the unaffected prostatic tissue and from it a false capsule is formed. It is through this plane of cleavage that the enlarged part of the gland can be easily enucleated. With the enlargement of the gland, changes may take place in the urethra, bladder, ureters, and kidneys

Urethral Changes. The prostate is usually described as having five lobes, anterior, posterior, middle, and two lateral. Simple enlargement affects either the two lateral lobes when it is usually symmetrical, or the middle lobe, or even more often the two lateral and middle lobes. The anterior lobe is only rarely affected and the posterior probably never As the apex of the gland is fixed and confined by the urogenital or triangular ligament, enlargement takes place upwards towards the bladder, and laterally. The urethra becomes compressed, elongated, and if the enlargement is asymmetrical, distorted, and it is this mechanical alteration which disturbs the act of micturition. Little indication can be obtained from the symptoms as to the size of enlargement. The internal meatus becomes altered Normally the opening is rather circular and the anterior and posterior commissures form segments of a circle and blend with the bladder wall. If the middle lobe is enlarged, a projection appears on the posterior commissure like a red hump. When both lateral lobes are enlarged, they come together to form a cleft or V at the anterior commissure.

Bladder Changes. With increasing obstruction to the outflow of urine, either from compression or distortion of the prostatic urethra or from a ball-valve action of an enlarged middle lobe, the bladder muscle works harder in order to empty itself, the muscle hypertrophies and the fibres stand out in criss cross bands like trellis work, called "trabeculation." Between the trabeculæ, weaknesses appear as depressions and form sacculations. Generally these remain small, but occasionally one herniates

completely through the muscle wall and forms a true diverticulum. As the enlargement upwards increases so does the obstruction and it becomes impossible for the bladder to completely empty itself. There is then residual urine after micturition, which leads to stasis when stones are more likely to form and infection to occur. The stones may form



Fig. 44. A grossly over-distended bladder showing dilatation of both kidneys and dilatation and tortuosity of the left ureter.

from any of the urinary salts, but in the sterile bladder, uric acid and calcium oxalate calculi are commonest, whilst in the presence of infection, the stone is usually formed of phosphates. The amount of residual urine bears no relation to the size of the gland.

Changes in the Kidneys and Ureters. The first effect of obstruction is seen in trabeculation, the second in residual urine, the third is when the upper urinary tract becomes dilated. This is probably due to the valve-like mechanism at the ureteric vesical orifice becoming incompetent. At any rate, the ureter dilates and becomes tortuous (*see* Figs. 44 and 45); the dilatation usually starts at the lower end, and increases to 0·5–1 cm. in diameter, by which time the pelvis of the kidney has also begun to dilate. Despite bilateral dilatation, renal function may, and usually does, remain quite good unless infection supervenes. Should this occur, there is an ascending bilateral pyelonephritis which quickly and markedly interferes with function and uræmia ensues.

Signs and Symptoms of Uncomplicated Enlargement. These fall into three groups: (*a*) local, (*b*) associated local, and (*c*) general.

infection is marked, it is unlikely that it can be eliminated unless the whole prostate is removed. In considering the radical operation, the possible and probable complications should be put to the patient.

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it usually is more obvious at the beginning or the end of micturition or may even occur independently of the act.

(*b*) *Associated Local Symptoms.* The occurrence of hæmorrhoids after the age of 50 always requires investigation, first of course, of the lower bowel but if no abnormality is found here, they may well be due to, or more often made worse by, straining, as the result of prostatic obstruction. Inguinal hernia may also be produced by such straining.

(*c*) *General Symptoms.* Apart from tiredness due to lack of rest from excessive nocturnal frequency, constitutional disturbance only results when the renal function has been seriously impaired. This occurs after long continued back pressure and especially if there is infection of the urinary tract. The patient feels unwell, unable to concentrate, and disinterested in his business. He may be irritable, drowsy through the day, and sleep badly at night. He complains of a bad taste in the mouth, lack of appetite, constipation, and flatulence. He may notice abdominal distension and experience pains in the abdomen especially on the right side. Occasionally, the face especially the nose, becomes red and this may give rise to embarrassment in a lifelong abstainer from alcohol! The cardio-vascular system is not noticeably affected by prostatic obstruction unless there is already a lesion of this system present. In the age group affected, the blood pressure is often raised, but does not seem more so in the presence of lower urinary obstruction. It is very unusual for simple enlargement of the prostate to alter the sexual function; exceptionally the libido is increased, and may then be reduced after removal of the gland.

Enlargement of the prostate gland is appreciated at digital rectal examination. The lateral lobes may be felt bulging into the rectum, rounded, smooth and elastic and at bimanual examination with the patient lying on his back, the whole gland may be felt, its size assessed and its mobility obtained.

Complications. The main serious complication is retention of urine. In long standing obstruction, there is always some residual urine but the term retention is reserved for the case when the patient is unable to pass any urine at all, or when there is still a large amount present after he has completed the act of voiding. There are two main types of retention—acute and chronic.

Acute Retention. In acute retention the patient is unable to pass urine after he experiences the desire. As time goes on the latter becomes worse and worse until ultimately there is a severe spasm of the bladder, and nothing is voided. The pain comes on at increasingly short intervals: the bladder becomes distended, tense, and tender, and the overwhelming desire is to empty it. As a rule the patient has had some warning that all is not well with the urinary tract; a history of increased frequency or of some difficulty can nearly always be elicited. The state of complete retention however, usually has some precipitating factor even though this may appear trivial as compared with the effect it has produced. Perhaps for reasons social or connected with his environment, he has been unable to pass water at the time the desire has occurred. It may be precipitated by a sudden rather unusual diuresis such as may be induced by over-indulgence in alcohol, a blood transfusion, or a mercurial diuretic. Confinement to bed for some other reason, medical or surgical, is a common cause of retention in a patient with enlargement of the prostate who has been able to compensate for the obstruction so long as he is mobile and able to try to pass water as soon as he feels the urge. Occasionally, a sudden severe hæmorrhage from the bladder, prostate, or upper urinary tract may produce a clot retention.

(*a*) *Local Symptoms.* These are mainly associated with the mechanical effect of the enlargement and there is a disturbance of micturition. The commonest symptom is increased frequency of micturition. This is not always due to the same cause. It may be present with a small middle lobe and no residual urine. If there is a large amount of residual urine, it may occur because the total capacity of the bladder is not much greater but it may occur with an enlargement of the lateral lobes, with or without much residual.



FIG 45 Fish-hook ureters seen with a chronically over-distended bladder.

The frequency may be mainly at night or both by day and at night. It may be associated with urgency and dribbling if a urinal is not immediately available. Difficulty is often a prominent feature and usually there is difficulty or hesitancy in starting the act. This difficulty may be influenced by strange surroundings, cold, or being at the head of a "queue," as after a meeting or social function There may be no difficulty in starting but the stream may have little or no force and the patient takes a long time to empty the bladder. This may not all be done at one time and the flow may stop and start again quite apart from the desire or voluntary effort of the patient. There may be a complete stoppage (*see* p. 113) or there may be incontinence especially at night. Occasionally, hæmaturia may be the presenting symptom and when this is due to prostatic enlargement

prostatic obstruction the gland is more often small and middle lobe enlargement seems more commonly to be present.

The Assessment of the Case with Prostatic Obstruction

There are certain cases which obviously need treatment. The man with acute retention is in pain and should be relieved. Opinion is divided as to the correct course to pursue in such a case. I have no doubt that, using full surgical precautions, he should be catheterized, the bladder emptied, and the catheter removed. In a considerable number of cases, when the bladder fills he will be able to void urine although perhaps at first with difficulty. He should be advised to have a prostatectomy at his early convenience. If he cannot initiate the act, the bladder should again be emptied and arrangements made for prostatectomy as early as is convenient. Some surgeons advise immediate prostatectomy in acute retention without any previous instrumentation. This is an attempt to diminish the risk of infection, which it may do. On the other hand, the patient with acute retention, by the time he reaches hospital, is tired, apprehensive, and from the business angle usually quite unprepared. He is often admitted at night when the usual theatre team may not be available. As the result of the retention there is always congestion in the prostate, which gives rise to increased bleeding at operation and any advantages of routine immediate intervention are out-weighed by the disadvantages. It may be however, that a catheter cannot be passed owing to prostatic congestion or that the bladder is full of clot and cannot be emptied. Under these circumstances, an emergency operation becomes necessary and it may well be that the prostate should be removed.

Chronic retention also calls for treatment but never immediate surgical intervention. Tests for renal function should be made. If the urine is clear of infection and of good concentration and if the blood urea is below 80 mg. per 100 c.c. an intravenous pyelogram should be done If satisfactory the obstruction is relieved by an operation of election without previous instrumentation, a cystoscopy being performed as the first part of the procedure. If on the other hand, the tongue is furred, the patient's mental outlook blurred, and the renal function grossly impaired, the urine will be of low specific gravity, may be infected, and the blood urea will be high. In such circumstances, bladder drainage should be instituted as soon as possible. Decompression of the bladder has up to recently been considered an essential in the treatment of such a case but many urologists now consider it neither necessary nor advisable In such a case, drainage is probably best by suprapubic cystostomy, but perineal urethrostomy and urethral catheter drainage are also employed. It is essential however, to ensure that diuresis continues during and after the drainage has been established. In cases with severe renal failure, this must always be effected by intravenous infusion as well as forced fluids by mouth—0·18 per cent Saline with 4 238 Dextrose is a useful routine solution but will be varied with the balance of the blood electrolytes (Also see Treatment of Uræmia, p. 59) Some urologists (Wells) consider that even these cases do not require preliminary drainage but should have the prostate removed when first operated upon. This reflects great credit on the efficiency of their after treatment, but in most clinics it is safer to attempt to restore the renal function before any major surgical intervention.

Now we come to the majority of cases, namely those whose symptoms do not suggest that immediate operation is necessary. The most important symptom of which to take note is difficulty in starting micturition and any patient who complains of this should be

On examination, such a patient is often quite fit although tired and apprehensive by the time he reaches surgical care. The bladder is distended, hard, and tender, and every few minutes there is an obvious spasm during which the patient is in great pain. The prostate although masked by the distended bladder, can often be distinguished per rectum when it will be enlarged, bi-lobed, smooth and elastic.

Chronic Retention. This term is reserved for the case when the bladder contains at least 250 c c. (10 oz.) after voiding. As the name implies, this has developed over a period of months or years. Some patients present with urinary symptoms. In others, the condition may be discovered accidentally or on routine examination in an attempt to discover the cause of lassitude and malaise. There are two main groups depending on whether the

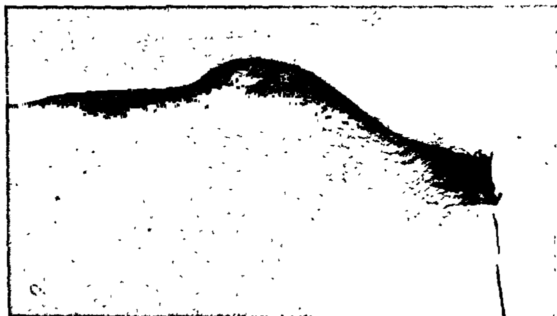


FIG 46. Chronic retention of urine.

renal function is adequate or not. In each group there may or may not be a disturbance of micturition. A man with several pints of residual urine in the bladder may pass urine 4–5 times a day and not at all at night, but it is much more likely that he will have increased frequency, and often may have urgency during the day and incontinence at night. The stream has nearly always lost its force and is usually a mere dribble. Bedwetting in a man who has been continent since childhood is always a serious symptom and requires full investigation. In the group with renal inefficiency the patient or his relatives will complain of his being unwell, that he has lost interest, is unable to concentrate, and no longer enjoys his family, his friends, or his common tastes

On examination the bladder may or may not be obviously distended (*see* Fig. 46). It is usually rather soft and may not be symmetrical, in which case it is often enlarged towards the right iliac fossa. There will be dullness on percussion in the suprapubic region and pressure here may give the desire to micturate and may even produce a little incontinence. On rectal examination, the bladder is usually felt pushing backwards into the rectum and often the prostate cannot be distinguished. In chronic retention due to

patient is fat and the cystostomy had been done low down. In such a case, there is often not much bleeding at the time of operation and should it occur, the cavity can be packed for 24 hours, with little disadvantage. The wound takes some time to heal of course, and the post-operative period is more unpleasant and tedious when compared with an operation with closure. A two-stage transvesical prostatectomy may also be safer when the surgeon is compelled to operate but is unfamiliar with other operative procedures and the few special instruments required for such are not available.

Method. A finger is introduced through the internal meatus, the anterior commissure is split, and the line of cleavage entered. If the prostate is large it may be necessary to introduce a finger of the other hand into the rectum to raise the gland and aid enucleation; any loose tags are removed and a large rubber tube (Marion's) is passed into the bladder. If blood wells up, the prostatic fossa is packed, otherwise the wound is closed around the tube which is at first allowed to drain into cellulose drainage.

Prostatectomy with Closure. In 1927 Harris introduced a suprapubic operation at which he controlled bleeding, with certain stitches at the bladder neck and closed the bladder. The trigonal flap is sutured to the prostatic fossa in the region of the divided urethra. Two lateral stitches control bleeding and two anterior stitches also aid in this and partly obliterate the prostatic cavity. A catheter is passed along the urethra, adjusted so that it is in the best position for drainage and held there by a long suture, the two ends of which come through the bladder and abdominal wall to be tied on the outside. This operation is still employed as the method of election after enucleation of the prostate in some clinics. Even when not used as a routine operation, it is useful when the bladder has to be opened on account of another pathological lesion, such as a papilloma or a diverticulum. By this method, Harris attained a mortality of under 3 per cent. Wilson Hey has also modified transvesical prostatectomy excising a large part of the trigone and meticulously occluding all bleeding vessels with diathermy.

Retropubic Prostatectomy. In 1945 Millin introduced a new approach to the prostate through the retropubic space. The method very soon became popular and is now used as the routine operation in many clinics in this country and also throughout the world. The anterior aspect of the prostatic capsule is exposed and opened. The line of cleavage is entered; the enlarged part of the gland is enucleated; the neck of the bladder is exposed and a triangle excised from the posterior commissure. Bleeding points are dealt with, a catheter is passed, and the prostatic capsule is closed. The advantages of this operation are several. The exposure is excellent so that all bleeding vessels can be easily seen, picked up, and occluded. The larger the prostate the better is this approach. The bladder wall is not incised A urethral catheter provides adequate drainage. The patient on the whole seems more comfortable during convalescence than after a transvesical operation and the mortality compares favourably with other operations.

Perineal Prostatectomy. The perineal approach to the prostate has never been popular in this country. Proust in France and Young in America developed this operation and it has still many adherents throughout the world. The patient is placed in an exaggerated lithotomy position. A curved or inverted V incision is made with the apex 3 cm. in front of the anus. By blunt dissection, the space behind the transverse perinei muscles on each side of the central tendon is opened up and the tendon divided near its anterior attachment. The apex of the prostate is exposed by drawing the triangular ligament and external urethral sphincter forwards and the rectum backwards. An incision

investigated further with a view to operation. Frequency is a nuisance and if combined with some other symptom such as poor stream or a little difficulty in starting, also merits attention. Obviously the symptoms are balanced against their duration and the age of the patient but worsening of frequency, in the absence of infection is an indication for intervention. It used to be considered that the measurement of residual urine provided an important hall mark. It may be necessary to pass a catheter to measure this in a doubtful case, but it is only one factor in the case. If the gland is enlarged and there is difficulty in starting the act of micturition, or if there is progressive worsening of the symptoms, operation is very probably necessary. An attack of acute retention is a warning which should be heeded, and marked frequency in itself always requires further investigation. This investigation consists of:

(1) Microscopic examination of a centrifuged deposit of the urine.

(2) Culture if any infection is present.

(3) Estimation of the blood urea.

(4) Intravenous pyelogram with a 30 minute picture before and after micturition. The latter may show a filling defect from the prostatic enlargement, residual urine in the bladder or trabeculation of the bladder wall, and the patient is then told that prostatectomy is advisable. As a first step a cystoscopy is nearly always indicated and as a usual practice it is wise to do this in the operating theatre with the patient anæsthetized and prepared to have the operative procedure then and there. It may not always be possible to say whether open operation or endoscopic resection is the best procedure in any individual case until this examination has been made, and then preparation will have been made for either to be carried out.

Differential Diagnosis

This may be difficult or obvious if routine tests are carried out. Chronic cystitis is shown by examination of the urine and cystoscopy. Stricture of the urethra is suggested by the history and inability to pass an instrument along the urethra and proved by urethroscopy. The diagnosis of muscle bar and fibrous bar bladder neck obstruction are discovered by elimination. Carcinoma of the prostate is usually discovered by rectal examination aided by cystoscopy but may require histological examination of a biopsy specimen. A neurological disorder is diagnosed by the presence of a specific disease and the absence of a mechanical cause.

The Operative Treatment of Simple Enlargement of the Prostate

Transvesical Prostatectomy. Effective operative treatment of simple enlargement of the prostate really began with this century In the latter part of the nineteenth century, some operations had been performed, mainly to remove the intra-vesical projection, by McGill in this country, and Fuller, Watson and others in America. Whilst Freyer may not have been the first to enucleate the whole of the senile enlargement transvesically, it was his skill and enthusiasm that showed that suprapubic prostatectomy could easily be done albeit with considerable mortality. There is still a place for this operation. If the bladder has had to be drained suprapubically, either on account of an intercurrent medical condition or because of renal insufficiency, there is much to be said for simple enucleation of the enlarged part rather than for a more elaborate type of operation, especially if the

Cold Punch Resection. The position of the patient and the important landmarks are similar to those in resection. The operator must be familiar with the view through a direct vision cystoscope. The instrument is positioned so that the distal edge of the fenestra is just proximal to the verumontanum. The knife is fully drawn back and is then pushed forward cutting off the tissue engaged in the fenestra. The cut with the punch is towards the bladder which is opposite to that with the resectoscope. Tissue is punched out until the capsule is reached which is usually apparent by seeing the rather pearly white transverse fibres. At the end of the operation bleeding is controlled by coagulating with a flexible diathermy electrode. A Foley catheter is introduced and free drainage is established.

After Treatment of Prostatectomy

(1) **Open Transvesical Prostatectomy.** Unless the bladder becomes filled with clot, irrigation is unnecessary and indeed harmful in the early stages. After the patient has

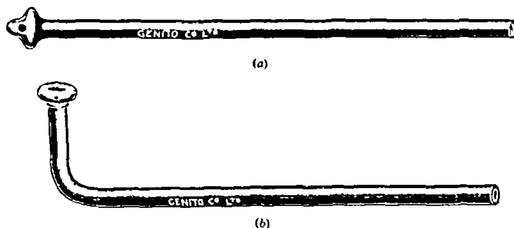


Fig. 47 (*a*) de Pezzer, and (*b*) Winsbury-White.

regained consciousness, drainage is collected in an Irving type of box. When bleeding makes it safe (2–4 days) the large Marion's tube is removed and a thinner straight tube is introduced into the bladder. When the wound has closed sufficiently around this tube, it is replaced by a self-retaining Malecot tube (5–7 days) (*see* Fig. 47). On the tenth day the suprapubic tube is removed and in some cases the patient is then able to pass urine, and the suprapubic fistula closes. More often, urine continues to drain suprapubically and if it is not passed normally in 48 hours, a urethral catheter is tied in until there has been no leakage for 4 days.

(2) **Closed Prostatectomy.** In the initial stages, the same post-operative treatment may be applied to all forms of prostatectomy, when the bladder has not been opened or has been completely closed. The indwelling urethral catheter is left in for a longer period, when the bladder has been opened as leakage often occurs if it is removed early. It is essential to ensure free drainage along the catheter and especially during the first 48 hours, the drainage must be inspected frequently by the nurse in charge of the case. If the control of bleeding has been adequate, and if there is a sufficient intake of fluid, the catheter drains easily. It may be that a small clot blocks its lumen and if so, this must be sucked out with a syringe. The catheter is removed when the urine becomes clear—in

is made in the urethra at this point over a urethral sound. A special prostatic tractor is introduced into the bladder and its butterfly wings opened out. With this, the prostate is drawn into the wound. The gland is still covered with the two layers of Denonvillier's fascia; the space between them (Proust's space) is opened into by making an incision on each side of the prostate and gently pushing back the posterior layer until the pearly white anterior layer is reached. An inverted V is now made in the posterior wall of the prostatic capsule starting at the apex, and when the flap is turned down, the line of cleavage between the false capsule and the enlargement is reached and the enucleation completed *en bloc*. The bladder neck can be grasped in tissue forceps and pulled down for inspection and all bleeding points are picked up and dealt with. A Foley catheter is introduced, the capsule is closed, and a perineal drain is left down to it.

There is no doubt that many clinics show a low mortality for perineal prostatectomy but there is always a risk even in the most expert hands, of incontinence and impotence, neither of which should occur with retropubic prostatectomy.

Endoscopic Prostatectomy. The approach to the prostate along the urethra, goes back to the early days of the nineteenth century when Guthrie and Mercier first employed cutting instruments to divide the bladder neck. Two main instruments are used at the present time: the resectoscope developed by McCarthy employs a wire loop through which passes a high frequency electric current by means of which strips are removed from the prostate. The cold punch with which the names of Braasch and Thompson are specially associated works on a different system. It employs a tubular knife which cuts strips off the gland. Much practice is required before either instrument may be employed with safety and efficiency.

Indications. In some clinics, notably in North America, surgeons have developed such proficiency in the use of endoscopic instruments that all but the largest glands are treated in this way. In this country, endoscopic resection is much more often reserved for the smaller, firm glands and for other types of obstruction such as muscle and fibrous bars and in obstruction from carcinoma of the prostate, which fails to respond to hormone treatment. Most British urologists believe that the larger glands are more safely and certainly dealt with by enucleation. On the other hand, there is little doubt the smaller enlargements are more efficiently dealt with by endoscopic methods.

Diathermy Resection. METHOD. The patient is placed in the lithotomy position and after the usual preparation, the instrument is passed The operator must be familiar with the view through a fore-oblique telescope. There are two most important landmarks—the bladder neck and the verumontanum, and these must be accurately identified at the commencement of the operation and their position verified from time to time during it. The verumontanum should remain intact and the risk of injury to the external sphincter is thereby greatly diminished The distance between the internal meatus and the verumontanum having been measured, the resection is commenced. The sheath is positioned so that it is on the bladder side of the verumontanum and the loop is extended to lie on the bladder aspect of the prostate The circuit is completed with the foot piece, the loop moved through the prostate, and a strip removed. This procedure is repeated methodically passing round from the posterior commissure laterally on each side until the middle and lateral lobes are removed Any spurting blood vessel is coagulated either with the loop or with a special coagulating ball electrode. The bladder is washed clear, all prostatic strips being accounted for and a Foley catheter is fixed in the urethra.

It is some weeks—4-6—before X-ray changes are apparent. There is at first a woolliness in the region of the symphysis with some decalcification of the bones. Later osteo-porosis is marked and the symphysis may become considerably separated.

Treatment. Treatment of this complication is extremely difficult. Pain is the outstanding symptom, and is often difficult to control. The patient is at first kept in bed and when allowed up a belt may help to relieve pain. Amongst treatments which have been tried and more often than not found ineffective are antibiotics, vitamins, ultraviolet light, short wave therapy, and X-ray irradiation. Claims for some relief are made after cortisone and recently open drainage has been advocated. Time however, seems to be the only fairly constant helpful factor as the majority ultimately recover after weeks or months of misery.

Fistula Formation. A suprapubic fistula nearly always means that there is persisting obstruction either at the bladder neck or in the urethra and clears up when this is treated. It may be due to the bladder becoming adherent to the back of the symphysis pubis or to prolapse of the bladder mucous membrane in a two-stage operation.

Post-operative Obstruction. (*a*) Obstruction at the bladder neck is usually due to the trigonal flap riding up and becoming adherent to the anterior commissure or front part of the prostatic capsule. The occurrence of such obstruction can usually be prevented by the excision of a triangle from the flap at the time of operation. Part of the prostatic capsule may remain as a loose tag or an adenoma may be left behind. A proper inspection of the prostatic bed after enucleation will avoid either of these. Such obstruction usually shows early—either there is a persistent leak or soon after discharge difficulty in micturition recurs. Sometimes the passage of urethral sounds to produce full dilatation of the bladder neck clears the obstruction especially if this is due to a band or portion of prostatic capsule. When the cause is a large trigonal flap or an adenoma, resection is usually necessary. If possible, this should be done endoscopically but if an instrument cannot be passed, the bladder must be opened.

(*b*) Stricture of the urethra may occur anywhere along its length if it is overstretched by passing too large an instrument Stricture occurs more frequently just in from the external urinary meatus at the fossa navicularis than at any other site. It shows itself within a few weeks, is quite narrow, and is very painful to dilate. It probably forms when a catheter too large for the urethra is left in post-operatively. A stricture may form at the proximal part of the anterior urethra. It is then most often due to a segment of membraneous urethra having been avulsed with the prostate at the time of operation. This injury may also produce incontinence since interference with the action of the external sphincter is then also likely. In such an injury treatment by repeated dilatations sometimes help Stricture just in from the external urinary meatus frequently clears up completely after a few dilatations. Stricture further along usually persists.

Post-operative Incontinence. This presents a great problem. Full dilatation of the urethra may help as may the practice of control exercises. Complete lack of control does sometimes persist and then a reefing operation such as described by Lowsley and by Millin should be tried If unsuccessful, a rubber urinal must be worn.

The Influence of Prostatectomy on Sex. It is probable that the patient is sterile after prostatectomy whatever the type of operation There is no doubt about it when bilateral vasectomy is performed. The libido and potency remain unaltered although the ejaculation is usually scanty.

2–4 days after endoscopic resection, in 3–7 days after retropubic prostatectomy, and in 10 days after transvesical prostatectomy with closure. Any other drain is removed on the fourth day. The older and more decrepit the patient, the earlier he is helped to become ambulant, and he is encouraged to exercise his limbs in bed as soon as he comes round from the anæsthetic.

Complications

Secondary Hæmorrhage. In most cases of prostatectomy there is a little bleeding between the eighth and fourteenth day after the separation of sloughs from the prostatic bed. As a rule it settles with rest and increased fluid intake. If the bleeding is severe, clots form which may not all pass and may cause retention. In this event, a catheter should be introduced as soon as possible and the clots evacuated by suction. This can always be done if the case is dealt with early enough, but if the clot has been in the bladder for some hours evacuation by suction may be difficult. In such a case, 20 per cent Pepsin in Glycerine should be injected into the bladder along a catheter and left for 1 hour. This sometimes breaks up the clot sufficiently for it to be sucked out. Failing this, the bladder is opened and the clot removed. Almost invariably when the bladder is completely emptied of clot, bleeding ceases or is of trivial account. Blood loss may have to be replaced by transfusion.

Infection.

(1) EPIDIDYMO-ORCHITIS would occur frequently if steps were not taken to prevent it. After prostatectomy by enucleation, the vas should always be divided on each side. Infection may still travel from the prostatic bed along the vas and then a swelling develops at the cut end in the scrotum. This does not give rise to the severe constitutional effect of an epididymo-orchitis (*see* p. 128). It should be treated by heat, a support, and the appropriate antibiotic.

(2) PYELONEPHRITIS. This is unusual but may occur. There is some malaise, and a swinging temperature but symptoms are often quite slight. It should be treated with the appropriate antibiotic.

(3) CYSTITIS. Some urinary infection is the rule after prostatectomy but in most cases this is sub-clinical and does not require treatment. If however, the urine is still infected six weeks after operation, treatment is necessary. A B. coli infection often responds to the administration of mandelic acid or a sulphonamide, but should these fail the sensitivity of the organism to antibiotics is determined and the appropriate one given.

(4) OSTEITIS PUBIS. Osteitis of the pubis appears to be of comparatively common occurrence in certain clinics and has been reported after each type of prostatectomy. It is said to be more common after the retropubic operation. It is thought to be an avascular necrosis from interference with the periosteum at the back of the pubis and amongst the causes given are infection in the prevesical space, extravasation of urine into this space, stripping or injury of periosteum by a boomerang needle. Diathermy used for coagulation of bleeding points in the retropubic operation may be a contributory factor to the occurrence of the condition.

Symptoms. The patient complains of pain in the pubic region soon after the operation. It may be very severe, and prevent sleep. It is made worse by standing. The pain may be present in both ischial tuberosities and may spread down both thighs.

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Carcinoma of the Prostate

This is a common condition. Clinically it occurs in about 20 per cent of those cases who present with prostatic symptoms but it seems fairly definite that a latent focus is present in the prostate far more frequently. Indeed in series of autopsies in which the prostate has been examined, histological evidence is reported in from 13 to 46 per cent of specimens. Malignant change may occur in any part of the gland but is commonest in the posterior lobe. It has been reported as occurring in young adults but is more common after the age of 50 years. It is uncommon to find histological evidence of carcinoma in the enucleated part of an apparently simple enlargement and whilst carcinoma does occasionally develop in the capsule after prostatectomy, this also is uncommon. In the large majority of cases, the growth has spread outside the capsule by the time the patient presents for treatment.

Signs and Symptoms. These fall into two groups: (1) When lower urinary obstruction is the main cause of symptoms. (2) When a metastasis is the main cause of symptoms.

(1) When lower urinary obstruction is the main cause of symptoms, the patient usually complains of frequency of micturition and increasing difficulty whilst occasionally there is pain. An important difference between simple enlargement and carcinoma is the mode of onset of symptoms. In the former the frequency and difficulty begin gradually and the patient usually has had them for several years and indeed cannot remember when they began. In carcinoma, on the other hand, the onset is quite sudden, not indeed overnight, but usually sufficiently definite for him to pin point the time to within a month. The only other condition which gives rise to such an acute onset is infection and in carcinoma, certainly prior to instrumentation, the urine is crystal clear. The patient may present with acute retention and much more rarely with retention with overflow. On digital examination, there is usually little doubt as to the diagnosis—the gland is enlarged and irregular and the nodules are very hard. It may be however, that the growth has not spread. The diagnosis then may not be so obvious but is suggested by feeling a small hard nodule in the posterior aspect of the gland, or by obliteration of the median groove between the two lateral lobes Hæmaturia is occasionally the first symptom and bleeding sometimes occurs apart from micturition. There may then be definite signs on cystoscopy, when an irregular nodular appearance is seen at the bladder neck, often accompanied by œdema, and is especially significant when seen to spread along the trigone.

(2) When a metastasis is the main cause of symptoms The commonest site for metastases from carcinoma of the prostate, is in bone and more especially in the lumbar vertebræ, in the pelvis, and in the femora. Then there is aching which may be quite severe, especially when the patient is ambulant. There may be compression of the body of one or more than one vertebra, leading to paraplegia and rarely a pathological fracture of the femur may occur. Sometimes the liver is the site of secondary deposits when a digestive upset or jaundice are the presenting symptoms. Less commonly, secondary deposits in the lungs give rise to persistent coughing, or hæmoptysis and are revealed on X-ray. Local extension of the growth or spread to regional lymph glands may give rise to pressure on nerves and may result in sciatica or may obstruct the iliac vein on one side producing a sudden œdema of one leg. With upward extension of the growth from the internal meatus along the bladder wall one or both ureters n

involved leading to destruction of the function of one or both kidneys. Downward extension through the triangular ligament is uncommon but may then spread into the erectile tissue of the penis, causing neoplastic priapism. Occasionally, the inguinal glands become enlarged and are infiltrated from lymphatic spread.

There may be no symptoms from the carcinoma and a nodule may be discovered on routine rectal examination which, on biopsy, proves to be malignant. The presence of carcinoma may be suspected when the adenomatous part of a simple enlargement is being enucleated and is found to be adherent or a focus may be discovered on routine histological examination in the centre of the part removed. The diagnosis may be obvious from digital or cystoscopic examination or may remain in doubt until a biopsy specimen has been examined histologically. At one time a raised acid phosphatase was considered to be an important test. It is very rarely helpful since so frequently the reading is normal. If it is raised, bony metastases are likely to be present.

Treatment. The only curative treatment which can be employed with a fair chance of success is the removal of the whole of the prostate gland. Radical prostatectomy through the perineal approach was employed by Young in America with some success and this method is being used at the present time in many clinics in that country. When first employed in this country, the results were bad, probably because of a wrong selection of cases, and the operation was given up. With the introduction of the retropubic approach by Millin however, attempts have been made to remove the whole gland in early cases, with some measure of success. The latter depends entirely on the extent of spread of the carcinoma. If still confined within the capsule of the gland, it is reasonable to expect that the neoplasm may be completely extirpated. Much of the success obtained in America is due to earlier diagnosis in that country. In Britain, probably only 1–2 per cent of cases are operable when first seen. In the United States however, the operability rate is increased to between 10 and 15 per cent of cases, and Kimbrough has been able to perform radical prostatectomy on as many as 50 per cent of his cases. Routine medical examinations are much more common in America than in this country. If a nodule is felt in the prostate, the patient is advised operation. Through a perineal incision, the gland is exposed, the nodule is removed, and a frozen section is made. If this shows malignant change, a radical perineal prostatectomy is then performed. The situation is not quite so straightforward as this however. Not more than 5 per cent of men over the age of 50 years are seen with prostatic carcinoma, the Registrar General's figures for 1947 show that less than 1 per cent of the deaths were from carcinoma, and yet histologically carcinoma has been found as frequently as in 46 per cent of cases, and not less than in 13 per cent when routine examination has been made of prostates removed at autopsy from cases without any clinical or macroscopical suggestion of malignancy. The only explanation of this discrepancy is that in a high percentage of cases with a histological focus of cancer in the prostate, the disease remains entirely inactive. If this is so, radical prostatectomy may be done in cases which will never become active if operation is always performed on account of a nodule discovered on routine examination.

Be that as it may, if there are symptoms of prostatic obstruction and a nodule suggestive of carcinoma is found in the gland, radical treatment should be instituted, certainly in men under the age of 60. In such circumstances, the perineal exposure appears to be very rational since the nodule can be examined histologically, as the first step in the operation. Recently, a less radical but perhaps quite effective attack has been made

by injecting a radio active gold solution into the prostate by the retropubic route (Flocks).

In the large majority of cases, the growth has spread beyond the confines of the gland before it is diagnosed, and then curative surgery should not be attempted. The work of Huggins and his associates showed that marked retrogression of carcinoma of the prostate both of the primary lesion and its metastases occurred after castration or the administration of œstrogen. Beneficial effect occurs within a few days and in 90 per cent of cases the local obstruction is considerably or completely relieved. If an œstrogen is being given, stilbœstrol is first tried in doses of 10 mg. three times daily. At the end of 4 weeks, this can be reduced to 5 mg. twice daily. Should stilbœstrol not prove effective, it is sometimes found that other preparations such as dienestrol and ethinyl œstradiol produce amelioration. Hormone therapy is almost certainly not curative although in the older age group, the growth may remain under control for upwards of 10 years. When the growth ceases to be controlled there may be a recrudescence of urinary obstruction but more often it is a metastasis which ceases to be controlled and pain then becomes a predominant feature. Should urinary obstruction return, it can be dealt with by endoscopic resection. Sometimes however, an instrument cannot be passed and if there is retention, suprapubic drainage must be established. There may be certain side effects from the administration of œstrogen. The breasts usually swell, become pigmented around the areola, and are tender. The testes if still present atrophy and indeed if they do not, castration is imperative. The penis becomes small, and the scrotum, especially the median raphe becomes pigmented. The libido is markedly diminished and should disappear. Some nausea and flatulence may occur and it has been said that the blood pressure may rise after prolonged administration, although this is unusual.

Sooner or later, there is a retrogression and if castration has not already been done, such should be performed. In some cases, the testis is the site of metastatic carcinoma. X-ray irradiation of painful bony metastases sometimes relieves pain but there is usually no permanent relief even from the combination of these treatments. In the absence of the testes the adrenal glands will produce androgens which may reactivate the carcinoma. In 1945 Huggins and his associates, performed bilateral adrenalectomy for a retrogressed case and since cortisone has become available, this operation has been fairly frequently done. It has been reserved for the patient in severe pain or when paraplegia has occurred. There is no doubt that some patients have been helped temporarily but it is probable that less benefit is derived from adrenalectomy in an advanced case of carcinoma of the prostate than in an advanced case of mammary cancer. It has recently been suggested that with further relapse, the pituitary gland should be removed. Surgical extirpation may well be the triumph of scientifically applied technical skill over common sense but destruction of the gland by irradiation may be more justifiable.

DISEASES OF THE GENITALIA

Abnormal Development of the Testes

ABNORMALITIES in the number of the testes are rare, absence of both or of one testicle has been reported as has the presence of a supernumary testis but this is very uncommon. Abnormalities in position, on the other hand, are comparatively common and may be

unilateral or bilateral. Normally, both testes are in the scrotum at birth, but in about 4 per cent of full term infants at least one gland has not descended. The majority of these reach the scrotum before or at puberty, but in the absence of treatment, there is permanent failure of testicular descent in about 2 adults per 1,000.

The testis may remain inside the abdomen, it may be retained in the canal, or it may be arrested in its descent from the external ring to the bottom of the scrotum. It may deviate from the track of its normal descent and come to lie in an ectopic position. When both testes are undescended, the scrotum is flat and undeveloped. If only one has descended, the other side although empty is usually quite well developed. The undescended testicle does not develop into the adult state after puberty, but remains small and flabby. It is difficult to feel in the inguinal ring but can usually be identified when outside it.

Causes of Non-descent. John Hunter put forward the view that this failure was due to an imperfection in the organ. This may be so in some cases but the failure of descent will in itself give rise to an imperfect organ. The endocrine function of the gland apparently persists in an abnormal anatomical position but spermatogenesis does not. There is little doubt that the lowered temperature of the scrotum provides an optimum situation for spermatogenesis. In the adult the temperature inside the peritoneal cavity is 2°C. higher than in the scrotal compartment and experiments have shown that in a testis transferred from the scrotum to the abdomen spermatogenesis ceases but will recommence if the gland is returned to its normal situation.

Heredity may play some part in abnormal descent. This factor is recognized as being of importance in animal genetics and occasionally a familial history of the anomaly can be elicited in the human. Some cases show a mechanical hold up from adhesions and occasionally from narrowing of the external ring. The vascular components of the cord are usually shortened—although not the vas—but this is more likely to be effect than cause.

Endocrine insufficiency is undoubtedly a cause in certain cases where the disability is bilateral but it is difficult to see how this can be a decisive factor in the unilateral case.

Failure of the Urogenital Union. In a small number of cases the epididymis and testis remain quite separate and there is neither macroscopic nor microscopic evidence that the urogenital union has taken place. This anomaly is rare but when it occurs it does so more often in the undescended organ.

Ectopia of the Testis. The testis is said to be ectopic if it lies in a situation other than in the line of its descent. Four varieties are described—superficial inguinal, perineal, pubic or penile, and femoral. Lockwood explained this abnormality by ascribing four tails to the gubernacular process which plays the part of a pathfinder in the descent of the testis from the abdominal cavity to the scrotum. If the continuity of the main process is broken, the gland follows the path of one of the tails and may then come to lie in its ectopic position. Lee McGregor describes a third inguinal ring at the entrance to the scrotum and in a series of examinations he has also found well marked perineal, superficial inguinal, and pubic pouches. If the continuity of the gubernacular track is broken the testicle will take the line of least resistance. If there is a wide way into the scrotum it may reach its normal position and remain there or it may pass on to the superficial perineal pouch and become a perineal ectopia. If the neck of the scrotum is closed by Lee McGregor's third inguinal ring, the testis will usually enter the superficial inguinal

pouch unless the opening of the pubic pouch is large and more inviting. No rational explanation has been put forward for the femoral ectopia when the testis passes through the crural ring to reach the thigh. The superficial inguinal position is the only common one and is usually easily recognized. The perineal position, normal in the pig, is not uncommon and not of much clinical significance in the human. The other ectopic positions are of extreme rarity.

Signs and Symptoms. Unless the testes are specifically examined, an abnormality in a child may be overlooked for years. If the condition is bilateral there may be stigmata of endocrine disorder but in the unilateral and ectopic disabilities there is nothing obviously abnormal. The majority of cases are discovered on routine examination. Occasionally a hernia may occur and draw attention to the anomaly, and torsion whilst rare is commoner in an undescended testis than in the normally placed organ. A hernial sac is present in 90 per cent of undescended testis but it is not very common in the superficial inguinal ectopia. An intra-abdominal testis may become strangulated at the internal ring by being suddenly prolapsed into the canal. This will give rise to sudden severe pain, nausea, and vomiting. Occasionally, the pain is so severe that the patient collapses. The pain is localized to the region of the internal ring. There is tenderness with guarding and a swelling can sometimes be felt just above Poupart's ligament. In such a case, the testis occasionally slips back into the abdominal cavity either spontaneously or after manipulation and there is then a complete relief from symptoms. In the adult, the patient may present with a neoplasm in the testis. When this is so, if the gland is intra-abdominal, metastases are always present. Neoplasm is much more common in an undescended than in a normally placed organ.

Intermittent Re-ascent of the Testis. The gland may be quite mobile and in certain individuals may be normally situated well down in the scrotum but intermittently it may go back into the inguinal canal. This especially happens on palpating the scrotum and is due to over-action of the cremasteric muscle. In such a case, the upward movement can usually be easily seen.

The Significance of the Abnormally Descended Testis. There is no doubt that the testis will not function properly unless it is in the scrotum. A man with bilateral undescended testis is almost certainly sterile. One undescended testis on the other hand, whilst it may diminish the cell count of the ejaculation by half, should not influence fertility if its counterpart is morphologically normal. A considerable proportion, if not the majority of unilateral cases descend before or at puberty and it is probable that they should be given a chance to reach the scrotum. Ninety per cent of undescended testis have a hernial sac and in many cases this is complete, and may require surgical treatment. An undescended testis appears statistically to be seven times more liable to be the site of a malignant tumour than a normally descended gland. An ectopic testis is more liable to be damaged from pressure. As a rule it is not accompanied by a hernial sac but the gland lies in quite a large vaginal process and is more liable to torsion.

Treatment of Abnormal Descent

ENDOCRINE THERAPY. This consists in the intramuscular injection twice weekly for 6 weeks, of an anterior pituitary-like hormone. It should not be given before the age of nine years and its administration should on the whole, be limited to the bilateral undescended testis. It is of no value in a case of ectopia and is rarely helpful in the unilateral

case. It may be used in the latter in order to increase the size of the gland prior to operation.

Orchidopexy. A very large number of different operations have been employed in the treatment of the undescended testis. There are two aims—one is to produce a cord of sufficient length so that the gland can be brought to the bottom of the scrotum without tension and the other is to keep it there. An ectopic testis has usually a cord of normal length and when dissected clear from its pouch can usually, easily, be brought into the scrotum. An intra-abdominal testis cannot be brought into the scrotum at one operation, but if the gland is in the inguinal ring the cord can often be lengthened without interfering with the many vascular components. All tight fibrous bands are carefully divided; a hernial sac if present is dissected clear, closed at the internal ring, and the excess removed and the cord is freed from the lateral pelvic wall by blunt dissection. The gland may now be brought down.

There are three main ways of fixing the testis:

(i) *Trans-scrotal orchidopexy of Ombredanne*. This uses the trans-scrotal septum as the retainer. A small opening is made in this septum and the gland is brought through into the contra-lateral scrotal compartment. I find this the simplest and most effective operation.

(ii) *The Keetley-Torek* operation is more elaborate and is a two stage procedure. At the first operation the gland is freed and brought down into the scrotum. An opening is made in the latter and also on the inner side of the thigh down to the fascia lata. The testis is brought out through the opening in the scrotum and anchored to the fascia of the thigh. The edges of the opening in the scrotum are sutured to those of the thigh. Three months later the testis and scrotum are separated from the thigh.

(iii) *External Anchorage*. There are numerous modifications of this. The testis having been brought into the scrotum, it is sutured to the skin of the scrotum and the ends of this suture are left long. Tension is now applied to this suture either by strapping it to the thigh, by fixing it to an elastic band, or by suturing it to the thigh.

THE RESULTS OF ORCHIDOPEXY. It is probable that the long term follow up of patients subjected to this operation, yield disappointing results. In some series there is a high fertility rate in the bilateral cases This may be so if only the superficial inguinal ectopias are included, but for cryptorchids the results in most series are not satisfactory.

Injuries of the Testis

Direct Violence. Considering their biological importance the testicles are in a very exposed position but this is to a considerable extent obviated by their mobility. They may be injured by direct violence, either open or closed, the former being almost confined to warfare and the latter mainly occurs in sport, especially in ball games. Such an injury is extremely painful, may produce profound shock, and the scrotum becomes very swollen and blue from extravasated blood.

Treatment. Closed injuries usually subside in due course. If surgical intervention is required orchidectomy is often necessary.

Torsion of the Testis or Spermatic Cord. This occurs more often in an incompletely descended organ and especially in infancy and childhood. The actual twist may occur between the testis and the epididymis or it may occur in the cord itself above the epididymis. Torsion takes place within the tunica vaginalis and as the venous return is

pouch unless the opening of the pubic pouch is large and more inviting. No rational explanation has been put forward for the femoral ectopia when the testis passes through the crural ring to reach the thigh. The superficial inguinal position is the only common one and is usually easily recognized. The perineal position, normal in the pig, is not uncommon and not of much clinical significance in the human. The other ectopic positions are of extreme rarity.

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affected than the body of the testis, it was unusual to isolate any special organism, and it was thought that the most likely cause was a virus.

Vaso-epididymal Reflex. Urine can pass from the prostatic urethra to reach the epididymis. It may be that a small quantity does so not infrequently and if the urine is sterile may not give rise to symptoms. In some cases however, this reflex produces severe pain along the vas and especially in the epididymis which may last for several hours or even days. It is unlikely that an isolated reflux will give rise to severe symptoms or indeed will be diagnosed but reflux of sterile urine may be the cause of recurrent testicular neuralgia and especially is this likely if some swelling of the cord and epididymis can be demonstrated.

Orchitis of Mumps. An acute infection, which affects the testis rather than the epididymis, occurs in mumps and much less commonly has been observed in other infectious diseases such as scarlet fever, malaria, influenza, and typhoid.

Signs and Symptoms. Beginning with discomfort in the scrotum the affected side rapidly becomes swollen, painful, and tender. In the pyogenic form due to gonococcus, staphylococcus, B. coli or streptococcus fæcalis, the swelling may become very large indeed and the scrotum becomes red, œdematous, and smooth and the normal corrugations disappear. There is always a small secondary hydrocele present but this may be so dominated by the inflammatory swelling as not to be noticed. In the severe case, the skin becomes fixed to the gland, an abscess forms and then fluctuation can be elicited. Should however, the swelling resolve under treatment, the first evidence of this is wrinkling of the skin of the scrotum, soon followed by desquamation. It may be possible to distinguish the swelling of the epididymis from that of the testis in the acute phase, but this is unusual. When the infection is of the epidemic type thought to be due to a virus, the swelling is much less and the epididymis is obviously more affected than the testis. The opposite is so in mumps, when the testis bears the brunt of the infection.

Treatment. Some cases form an abscess which requires incision and drainage, others slowly or quickly subside. In all cases there is some residue, the least being a nodular thickening of the epididymis. In the worst of cases there is atrophy of the testis, and this is common after the orchitis complicating parotitis. Support to the scrotum with the local application of heat—but sometimes cold—makes the patient more comfortable. Sulphonamides and antibiotics do not markedly influence the progress of the condition but if the organism and its sensitivity are known, should be given. The administration of an œstrogen sometimes helps. It has been suggested that early incision of the epididymis—so-called decompression—will shorten the convalescence but this does not always prove effective

Sub-acute or Chronic Epididymo-orchitis. The commonest cause of a chronic infection is tuberculosis, although a virus infection may give a very similar clinical course in the first few weeks. Genital tuberculosis is a disease of young adults. It is rare in children and when it occurs in the older group is usually a flare up of a latent infection. There is probably always a co-existent infection in the prostate and usually one if not both vesicles is palpable and clinically involved. If observed before the condition has become fully developed, the globus minor is usually the first part to be affected which suggests that the spread has been along the vas. This globus becomes enlarged, firm, and a little tender and very soon so does the globus major. The whole cord is at first a little thickened but

impeded before the artery, the part distal to the twist becomes engorged, blue, and plum coloured. With a complete twist, if nothing is done, the testicle becomes gangrenous and atrophies, and this usually occurs before surgical intervention has taken place.

Signs and Symptoms. There is a sudden pain in the groin, often accompanied by vomiting. If the patient is an infant, there will be a fit of crying. On examination there is a tender, firm swelling in the groin and the right side of the scrotum is empty. The differential diagnosis must be made from strangulated hernia, epididymo-orchitis, and the orchitis of mumps.

Treatment. If operation is sufficiently early, the testicle may be still viable and this is especially so if the twist is not complete. The structure is untwisted and the testicle is fixed to the scrotal wall with one or two catgut sutures. If, as is much more likely, operation has been delayed for several hours, an irreversible change will have taken place and an orchidectomy should be performed. The testicle on the other side should be carefully examined and if it is unduly mobile, it should be fixed.

Torsion of the Appendix of the Testis. The appendix of the testis or hydatid of Morgagni is a small "polyp" attached to the upper pole of the testis and is the remnant of the fimbriated end of the Mullerian duct. The only clinical significance of this structure is that occasionally it becomes twisted at its base and its end swells up. This may be quite painful and a small rounded swelling, acutely tender, may be felt sitting on top of the testicle. When diagnosed, the testis is exposed by opening the tunica vaginalis and the swollen structure is removed.

Infections of the Testes, Epididymis, Vasa Deferentia, and Seminal Vesicles

Infection may affect the testis together with the whole of its duct system or it may be confined mainly to one part.

Epididymo-orchitis. An infection rarely occurs which is entirely confined to the epididymis or to the testis; in certain infections, both appear to be involved to much the same extent whereas in others, the infection is preponderant in either the testicle or the epididymis. Much the commonest route along which the infection arises is by the vas, and this may be through the lumen or along the lymphatics. Certain infections however, do occur in the testis which appear to be blood borne and in which there is no evidence of such a spread as, e g. in the orchitis of mumps.

Acute Epididymo-orchitis. This is a sudden infection which usually reaches the epididymis and testis via the lumen of the vas There is marked swelling of the epididymis and testis which may become 6–8 times normal size Whilst the testis to a large extent, retains its shape, at the height of the attack, with this amount of swelling, it cannot be distinguished from the epididymis. The commonest site of origin of the infection is in the posterior urethra, and acute epididymo-orchitis was a fairly common complication of a gonococcal urethritis which had been neglected or had been badly treated. Prior to routine ligation of each vas deferens, it occurred in 30 per cent of patients subjected to prostatectomy. It still sometimes develops after instrumentation of the urethra in the presence of infection and has followed a digital examination of the prostate when there has been an acute prostatitis. Common infections other than gonococcal are from B. coli, staphylococcus aureus, or streptococcus fæcalis. A less severe infection was of fairly common occurrence in the Services during the 1939–45 war. Indeed it was so prevalent in certain regions as to be almost epidemic. The epididymis was much more

sometimes occurs before puberty and may then be a cause of sexual precocity. It is a well-circumscribed tumour within the substance of the testis and has a yellowish-brown colour on section from the presence of lipoids in the cells. Histologically the cells are variable and of no particular shape, with large eccentric nuclei. Most of these tumours are benign but in some cases they have given rise to metastases and are therefore malignant.

Malignant Neoplasms of the Testis. The large majority of tumours of the testis are malignant and indeed any tumour should be considered to be so until this has been disproved by histological examination. The testis is not a common site of tumour formation but most neoplasms in this situation are highly malignant. If treated early and adequately, however, the prognosis for certain types of new growths is quite good. Several classifications of testicular tumours have been suggested but that of Gordon Bell is widely accepted in this country as being the most satisfactory. There are two main groups—Teratoma and Seminoma—and these account for 90 per cent of neoplasms. Amongst the remaining 10 per cent adeno-carcinoma of the rete testis is the commonest and sarcoma and carcinoma of the seminiferous tubules are very occasionally encountered.

Teratoma of the Testis. This is a curious tumour which is seen most often in the age group 20–40 years. It varies tremendously in its malignancy and may pursue a benign or relatively benign course, or may be highly malignant, metastasing early, with a very grave prognosis. It has been thought to arise from a totipotent cell and Bell described four groups of tumour—(i) Heterogenous containing epidermal, endodermal, and mesodermal elements. (ii) With epidermal preponderance. (iii) With endodermal preponderance. (iv) With mesodermal preponderance.

(i) *Heterogenous.* Cystic, fibrocystic, or solid tumours may be found in this group. They may be quite bizarre containing bone, cartilage, teeth, and hair.

(ii) *With Epidermal Preponderance.* This group includes the dermoid cysts, squamous cell carcinoma, and chorion-epithelioma. The latter is the most malignant of all testicular tumours and there may be widespread metastases especially in the liver and lungs with gynecomastia whilst the primary lesion may still be quite small, only 1–2 cm. in diameter and easily overlooked.

(iii) *With Endodermal Preponderance.* In this group which is the least common, the structure of the neoplasm is mainly glandular.

(iv) *With Mesodermal Preponderance* This is the commonest form and in this group most tumours contain much cartilageous tissue and there may also be bone, muscle, and fat

Seminoma. This occurs in the rather later age group 30–50 years but may occur in the elderly as well as in adolescence. It is thought to arise from a germinal cell and may grow slowly when metastases are late in developing. It is this type of tumour which more frequently affects an abnormally descended testis or one which has been subjected to trauma or infection. When cut, the tumour is solid, firm, and greyish white. The cells are large with clear cytoplasm and resemble spermatocytes.

Adeno-carcinoma of the Rete Testis. This accounts for 2–3 per cent of cases and whilst uncommon, deserves some special mention. It occurs in the posterior part of the body of the testis near the mediastinum. The tumour is at first small and difficult to distinguish. It frequently gives rise to pain. Histologically, it is an adeno-carcinoma with a papillary arrangement of cells projecting into cystic spaces.

later the vas is sometimes felt to be irregularly enlarged and gives rise to the so-called beaded effect. Such a finding is by no means constant however. There is fairly often a small secondary hydrocele. The infection in the epididymis breaks down and caseates. Very occasionally, calcification occurs and the condition then usually becomes quiescent, but more often an abscess cavity lined by granulomatous tissue forms. In the course of time, this abscess bursts into the scrotum, the skin of the latter becomes attached to the back of the epididymis, and later breaks down resulting in a posterior sinus.

A tuberculous epididymis is therefore a very chronic condition. In the course of time it is felt as a hard craggy irregular mass and there is evidence elsewhere in the body of a tuberculous lesion, which of course may be quiescent.

Treatment. If the condition is tuberculous, the same principles are applied as in the treatment of urinary tuberculosis. Young's operation of bilateral orchidectomy, vasectomy, vesiculectomy, and prostatectomy is no longer performed. The patient is put on supporting treatment with streptomycin, para-amino salicylic acid, a hydrazide of isonicotinic acid, and on a sanatorium regime. It is claimed that many, if not the majority of cases can be completely controlled by this treatment and in the younger age group, it is the method of choice. In the older age group and especially if a sinus presents, a cure can be affected more quickly if surgical removal of the testicle or the epididymis is performed, after 1–2 months of treatment.

Vesiculitis. An acute vesiculitis usually occurs in association with a prostatitis or cystitis.

Signs and Symptoms. The principal complaint is pain in the rectum and perineum with malaise, frequency of micturition, and pyrexia. Sometimes all the symptoms are abdominal and the patient then complains of lower abdominal pain passing into the iliac fossa. The affected vesicle is acutely tender when tense, but it may not be possible to distinguish the actual vesicle. The diagnosis must be made from acute prostatitis and cystitis, and if the right vesicle is affected, acute appendicitis. The patient should be put to bed and made to drink large quantities of bland fluids Alkalis are given by mouth and, by examination of the urine, the infecting organism may be determined. The appropriate sulphonamide or antibiotic should then be administered.

Chronic Vesiculitis. This may be tuberculous or non-specific.

(*a*) Tuberculous Vesiculitis This rarely gives rise to special symptoms but is part of a genital infection, the most important manifestation of which is usually in the epididymis.

(*b*) Non-specific Vesiculitis. This is not common but may be a most troublesome complaint. It is usually due to a staphylococcal or coliform infection and gives rise to perineal and rectal pain, aching testicles, and hæmospermia. The vesicle and prostate should be massaged and a culture made. If the organism can be isolated it should be treated appropriately and often stilbœstrol given for 3 months may be useful ancillary treatment. If no relief can be obtained medicinally, vesiculectomy—which is quite an undertaking—must be contemplated

Tumours of the Testis and Epididymis

Benign Neoplasms of the Testis. Benign growths of the testis are rare—adenoma, fibroma, or hæmangioma have all been found. A less uncommon type is the interstitial cell tumour, which often appears to be a hyperplasia of the interstitial cells of Leydig. It

sometimes occurs before puberty and may then be a cause of sexual precocity. It is a well-circumscribed tumour within the substance of the testis and has a yellowish-brown colour on section from the presence of lipoids in the cells. Histologically the cells are variable and of no particular shape, with large eccentric nuclei. Most of these tumours are benign but in some cases they have given rise to metastases and are therefore malignant.

Malignant Neoplasms of the Testis. The large majority of tumours of the testis are malignant and indeed any tumour should be considered to be so until this has been disproved by histological examination. The testis is not a common site of tumour formation but most neoplasms in this situation are highly malignant. If treated early and adequately, however, the prognosis for certain types of new growths is quite good. Several classifications of testicular tumours have been suggested but that of Gordon Bell is widely accepted in this country as being the most satisfactory. There are two main groups—Teratoma and Seminoma—and these account for 90 per cent of neoplasms. Amongst the remaining 10 per cent adeno-carcinoma of the rete testis is the commonest and sarcoma and carcinoma of the seminiferous tubules are very occasionally encountered.

Teratoma of the Testis. This is a curious tumour which is seen most often in the age group 20–40 years. It varies tremendously in its malignancy and may pursue a benign or relatively benign course, or may be highly malignant, metastasing early, with a very grave prognosis. It has been thought to arise from a totipotent cell and Bell described four groups of tumour—(i) Heterogenous containing epidermal, endodermal, and mesodermal elements. (ii) With epidermal preponderance. (iii) With endodermal preponderance. (iv) With mesodermal preponderance.

(i) *Heterogenous.* Cystic, fibrocystic, or solid tumours may be found in this group. They may be quite bizarre containing bone, cartilage, teeth, and hair.

(ii) *With Epidermal Preponderance.* This group includes the dermoid cysts, squamous cell carcinoma, and chorion-epithelioma. The latter is the most malignant of all testicular tumours and there may be widespread metastases especially in the liver and lungs with gynecomastia whilst the primary lesion may still be quite small, only 1–2 cm. in diameter and easily overlooked.

(iii) *With Endodermal Preponderance.* In this group which is the least common, the structure of the neoplasm is mainly glandular.

(iv) *With Mesodermal Preponderance.* This is the commonest form and in this group most tumours contain much cartilageous tissue and there may also be bone, muscle, and fat.

Seminoma. This occurs in the rather later age group 30–50 years but may occur in the elderly as well as in adolescence. It is thought to arise from a germinal cell and may grow slowly when metastases are late in developing. It is this type of tumour which more frequently affects an abnormally descended testis or one which has been subjected to trauma or infection. When cut, the tumour is solid, firm, and greyish white. The cells are large with clear cytoplasm and resemble spermatocytes.

Adeno-carcinoma of the Rete Testis. This accounts for 2–3 per cent of cases and whilst uncommon, deserves some special mention. It occurs in the posterior part of the body of the testis near the mediastinum. The tumour is at first small and difficult to distinguish. It frequently gives rise to pain. Histologically, it is an adeno-carcinoma with a papillary arrangement of cells projecting into cystic spaces.

Secondary Neoplasms. Metastases are not very rare in the body of the testis. The primary neoplasm is then often in the prostate but it may be a carcinoid of the appendix or an adeno-carcinoma of a kidney.

THE COURSE AND PROGNOSIS OF TESTICULAR NEOPLASMS. Without treatment testicular growths increase in size and for some time are confined within the tunica vaginalis. Ultimately they burst through the tunica and ulcerate and herniate through the skin.

Distant metastases may occur early or late. The commonest spread is lymphatic along the cord to the iliac lymph nodes and from there to the para-aortic glands. Spread may also be blood borne and deposits occur in the lungs or the brain. With treatment, especially for the seminoma, orchidectomy combined with irradiation gives a survival of 45 per cent for 5 years, and of 24 per cent for 10 years (Gordon-Taylor). Adeno-carcinoma of the rete testis is highly malignant and the results from radiotherapy are poor. In chorion-epithelioma metastatic deposits occur early and treatment is of little avail.

Signs and Symptoms. A swelling in the testicle is usually discovered accidentally by the patient Attention may be drawn to it after an injury and the latter may have had some part to play in its rate of development. It is unusual for pain to occur in the early stages although attention may be directed to the testis on account of dragging or an ache after standing or walking The tumour varies tremendously in size and may be from 1 cm. in diameter to the size of a coconut. It is usually hard and solid to feel, but exceptionally may be soft or cystic in consistency. There is often a small hydrocele—a secondary hydrocele—of the tunica vaginalis and this may transilluminate or may be dull when there has been an extravasation of blood. The tumour may be smooth and this is so in the early stages but later becomes irregular or nodular. It is rarely tender. It may be very difficult in the early stages to distinguish between a tumour of the upper and lower pole of the testis and a thickened epididymus. A swelling half-way down in the posterior surface of the testicle is far more likely to be testicular than epididymal.

Treatment. When a neoplasm is thought to be present the testicle must be removed. It is highly improbable that it is benign and such can only be proved by histological examination. If there is some doubt as to whether the swelling is in the testis or epididymis operation should be performed, the tunica vaginalis opened, and the gland and epididymis examined. There is then no doubt as to where the swelling is situated. If it is in the body of the testis an orchidectomy must always be done. If in the epididymis, epididymectomy may be considered if the condition is thought to be inflammatory, but if neoplastic, orchidectomy is again necessary.

If the tumour is shown histologically to be a seminoma, a course of X-ray therapy must be given. It should also be given for a teratoma, although less likely to be helpful.

Gumma of the Testis.

At one time a common condition, gumma of the testis is now rarely seen and simulates a neoplasm Usually only one side is affected and although the epididymis may be involved, the condition is more often confined to the body of the testis. Very occasionally, a gumma may occur in the substance of the cord.

Signs and Symptoms. A swelling is usually noticed accidentally, and it gradually and painlessly increases in size. It is hard, not tender, and retains the contour of the testes. The Wassermann reaction is positive in 85 per cent of cases. Very occasionally, the gumma breaks down and discharges. The sinus opens in front of the testis and can

then be distinguished from that resulting from a tuberculous epididymitis, which opens behind.

Infarction of the Testis

Infarction of the testis follows thrombosis in a testicular vessel. It is an uncommon condition which occurs for no apparent reason in young adults. The testis is rather plum-coloured, there is a small blood-stained hydrocele of the tunica vaginalis, and the cut surface of the gland shows extravasated blood. The clinical signs and appearance of the testis are rather similar to that produced in torsion of the cord, and the differential diagnosis may only be made at operation.

Signs and Symptoms. There is a sudden severe pain usually beginning in the iliac fossa and spreading to the affected testis. This often occurs at rest and indeed may develop through the night and awaken the patient. At first, there is little or no swelling but during the next 24 hours, the testis increases to two or three times its normal size. The gland remains spheroidal in shape, the temperature is only very slightly raised and the white cell count is normal. If left alone, the swelling slowly subsides over the next six to eight weeks, and ultimately the testis is completely atrophied.

Treatment. It is likely that the testicle will be explored and if so, orchidectomy should be performed since the convalescence will then be considerably shortened.

Tumours of the Epididymis, Spermatic Cord, and Seminal Vesicle

New growths arising from these structures are uncommon. The majority are mesoblastic and are usually benign.

Tumours of the Epididymis. These are very uncommon. Fibroma and fibromyoma have been described as have also sarcoma, fibromyosarcoma, and secondary melanoma.

Tumours of the Spermatic Cord. Lipoma and fibro-lipoma of the spermatic cord are not uncommon, and a lipoma is not infrequently seen at the fundus of a hernial sac.

Signs and Symptoms. A swelling is either discovered accidentally or at a routine physical examination. It is not painful nor tender and when in the epididymis may be difficult to differentiate from an inflammatory swelling.

Tumours of the Seminal Vesicle. A neoplasm arising in a seminal vesicle is extremely rare; less than thirty have been reported in the literature. Benign tumours are especially uncommon and carcinoma is the most frequent neoplasm.

Signs and Symptoms. These tumours give rise to disturbance of micturition—frequency and difficulty being the two commonest—and the patient may present with complete retention of urine. A neoplasm of a vesicle may be a rare cause of hæmospermia.

Cystic Swellings of the Scrotum

Congenital. There are certain embryological remnants which may undergo cystic degeneration—the hydatid of the testis and that of the epididymis, the paradidymis or organ of Giraldes, and the vas aberrans of Haller arising from the first part of the spermatic duct. These cysts are mainly of academic interest, probably remain small, and are uncommon They can be distinguished from a spermatocele and from a hydrocele because they contain a clear watery fluid.

Spermatocele. This is a retention cyst formed by obstruction in and dilatation of a vas deferens. It is occasionally seen soon after puberty and may then be due to partial

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The Course and Prognosis of Testicular Neoplasms. Without treatment testicular growths increase in size and for some time are confined within the tunica vaginalis. Ultimately they burst through the tunica and ulcerate and herniate through the skin.

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of the embryological remnants and only if a hydrocele has become lobulated is it possible to feel the testicle distinct from it. The ultimate proof may be obtained by tapping. Hydrocele fluid is yellow, spermatocele fluid is opalescent, and cystic fluid is clear.

Treatment. Palliative treatment consists in tapping, and withdrawing the fluid contents. In the elderly with a large swelling which has become a nuisance, this may suffice. It will have to be repeated at intervals varying from a few weeks to a few months, depending on the speed of refill. *Method:* After cleansing the skin of the scrotum, the hydrocele is made tense and a sterile trocar is stabbed into the sac. A route can be planned to avoid any superficial vessel which can be seen on making the swelling tense, and thus bleeding should not occur. Emptying is assisted by keeping up pressure on the scrotum until all the fluid has been evacuated. This form of treatment is entirely palliative. The curative treatment of hydrocele is either by injections or by operation.

(*a*) INJECTION TREATMENT. The hydrocele is tapped and when emptied a sclerosing liquid is injected—5 ml. of sodium morrhuate or 5 ml. of ethamoline are most often used. After injection the scrotum is massaged so that the sclerosing fluid may contact as much of the lining wall as possible. The hydrocele begins to fill up again quite quickly, fresh fluid has usually formed in a week, and the process of emptying and injecting is repeated, and may require 3 or 4 treatments. The method is rather painful and somewhat uncertain and if it fails, operative treatment is rendered a little more difficult.

(*b*) SURGICAL TREATMENT. The hydrocele is exposed through an incision in the scrotum and the sac opened. If large, much of the wall is excised but if small the testis is invaginated and the edge of the tunica vaginalis approximated behind the epididymis with one or two sutures.

DISEASES OF THE PENIS AND URETHRA

CONGENITAL ANOMALIES OF THE URETHRA

Valves in the Posterior Urethra. These are an important cause of lower urinary obstruction in the infant. The large majority of such valves are found distal to the verumontanum but rarely they may be proximal to it. These valves produce obstruction which is usually severe and then requires treatment in childhood. More rarely, if less complete, the patient may go untreated until adult life. Through a hypogastric exposure, the valves are reached by a vertical incision which starts in the lower segment of the bladder and passes downwards to open up the prostatic urethra. They are usually fairly readily identified and are then removed under direct vision. With suitable instruments, they may be removed endoscopically through a perineal urethrostomy.

Diverticulum of the Urethra. This is very uncommon. In the male, it is more often found in the anterior urethra and then usually opens into the canal by a wide mouth. In the posterior urethra it may be due to dilatation of the prostatic utricle or to an ectopic opening in a ureter which ends blindly.

In the female, diverticulum of the urethra is a little more common than in the male, but it is doubtful if it is then congenital in origin. It is exceptional to find it in children or in the nulliparous, and is sometimes associated with a stricture of the urethra or with infection.

Hypospadias. In this deformity the urethra opens proximal to its usual situation. Three grades are described:

(*a*) Glandular, (*b*) Penile, and (*c*) Perineal.

failure of the urogenital union. In the large majority of cases however, the patient is over 40 years when first seen and quite often the swelling is discovered at a routine physical examination. It may be single but more often there are several cysts, although only one may be large. The testicle lies below and in front of a spermatocele and can always be distinguished, even when there are several spermatoceles of much the same size as the testicle, since it does not transilluminate. A spermatocele usually remains comparatively small with a diameter of less than 3 cm. Occasionally one may reach considerable size however, and contain 500 c.c. (17 oz.). When of this size it constitutes a nuisance to the patient and may be tapped (when it quickly refills) or may be excised. It is rare to find one recur when the whole epididymis is removed. The fluid in a spermatocele is opalescent and contains spermatozoa.

Hydrocele of the Tunica Vaginalis. This may be (1) primary when it is usually chronic, insidious, and often large or it may be (2) secondary when it is acute and usually small.

(1) Primary or Idiopathic Hydrocele. This usually begins insidiously in a healthy individual and the testis on the affected side is normal. The lining is usually smooth but in some cases it becomes thickened and a little rough from deposited fibrin. Occasionally, part of the wall becomes calcified. The fluid in the sac is normally clear and yellow but may be altered by injury or after tapping, when, depending on the amount of bleeding, it may be thin and brown, or thick and of chocolate colour. Occasionally, there are small loose fibrin bodies in the sac rather like melon seeds.

Congenital Hydrocele. This is really a patent infantile funicular process communicating with a peritoneal cavity which contains fluid.

Hydrocele en bissac. A patent processus vaginalis rarely may become closed at the internal ring only. If a hydrocele forms, part of it may lie deep to the transversalis and form a sort of hourglass cyst, one part in the scrotum and the other and larger part bulging into the peritoneal cavity. There is a narrow communication between the two compartments along the inguinal canal.

(2) Secondary Hydrocele. This usually forms in association with disease or injury of a testis. It may be found with a gumma, with a neoplasm, or with an infection especially a tuberculous epididymitis. If all the spermatic veins are divided in an attempt to cure a varicocele, a hydrocele often results In the treatment of an indirect inguinal hernia with a complete infantile process, the lower end is left surrounding the testis. If it is closed, a hydrocele commonly forms Secondary hydroceles are usually much smaller than are the idiopathic, are often soft, and the testis can then be easily palpated through the sac.

Signs and Symptoms In primary hydrocele the patient presents on account of the size of the swelling. This is oval or pear shaped with the narrower end pointing upwards. It is smooth, tense, freely movable, fluctuant, and not tender. It is always possible to get above the swelling except if it is of the congenital or en bissac type. It can be transilluminated unless the walls are much thickened or unless it contains blood. The testis cannot be felt unless the hydrocele is very lax but on transillumination its shadow can be seen usually in the lower posterior quadrant. A hydrocele which has been tapped may become loculated and then its rounded, smooth character may alter

Differential Diagnosis. A testicular swelling is solid, and does not transilluminate. It is not possible to get above a hernia which, unless strangulated, also has an impulse on coughing. The testis can be felt apart from a spermatocele or from a cyst arising in any

the urethra is a gutter, and the patient is incontinent. There is often wide separation of the two pubic bones in the mid line.

Treatment. The minor degrees are better left alone. Several operations have been designed to relieve the incontinence associated with the severe degree. Young excised most of the urethra leaving only a narrow strip. Conservative reconstructive operations are unsuccessful in most surgeons' hands, and a uretero-colic anastomosis is eventually necessary.

Congenital Anomalies of the Penis

Anomalies of the Prepuce

Normally, the prepuce covers the glans penis but can be easily retracted. It may be too long or too tight. In the latter case, it cannot be retracted and infection may occur leading to balanitis. In either instance, circumcision should be performed.

Para-urethral Ducts

An accessory opening on the glans is not exceptionally rare. Such an opening may communicate with the urethra but more often ends blindly. The duct may be quite long and is then usually on the dorsum of the penis. Prior to the introduction of specific treatment for gonorrhœa, such a duct sometimes became the stie of a chronic infection which was extremely difficult to eradicate. If a non-specific infection occurs in a long duct, and cannot be cleared up, it may be necessary to perform a complete excision.

Injuries of the Urethra

These may be open or closed. Open injuries are nearly always associated with warfare and are rarely encountered in civilian practice. Closed injuries are commonly met with in wartime, but may also occur in civilian practice.

Open Injuries of the Urethra. These are usually due to wounding with a missile and much less commonly to a bayonet wound involving the external genitalia. Most of the wounds are complicated by injury to some other important structure and may have passed through a buttock, thigh, the pelvis, pelvic viscera, or the scrotum and quite frequently one or both of the testicles is severely injured. The extent of the injury is usually determined on examination of the patient.

Treatment. A suprapubic cystostomy must be done in all except the most trivial of injuries. Subsequent treatment depends on the amount of actual tissue loss. The site of injury is exposed and a surgical toilet of the wound undertaken. The ends of the urethra are identified, any ragged edge excised, and the continuity of the canal is restored. It is helpful to do this with a catheter in the urethra but such should be removed when the two ends have been joined together. The bladder is drained for 14 days or until the perineal or penile wound has healed. If there has been much destruction of tissue, some plastic restoration which may be quite extensive, is required.

Closed Injuries. These are divided into two groups (1) rupture of the prostatic urethra or intra-pelvic injury and (2) rupture of the anterior urethra or extra-pelvic injury.

(1) Intra-pelvic Rupture of the Urethra. This is always the result of a severe injury and is usually associated with fracture of the bony pelvis. The rupture takes place at the apex of the prostate, but the urethra is not always divided at the same level. Sometimes the pull on the prostate draws up a segment of the membranous urethra as well

Glandular Hypospadias. The external meatus is anywhere between its normal position and the junction of the glans with the body of the penis. This degree is of little clinical significance except that there is an increased liability to contract a urethritis. In the normal urethra the distal centimetre is lined by squamous cell epithelium and this is thought to be more resistant to infection than is transitional cell epithelium which lines the remainder of the urethra. The urethra, in hypospadias, is lined throughout with transitional cell epithelium.

Penile Hypospadias. The opening may be anywhere along the level of the shaft of the penis and the further back this is, the greater is the deformity. If well forward, the penis may be quite well formed and only slightly curved on itself, but far back the organ is small, the corpora cavernosa are ill developed, and the penis has a marked downward curve which becomes particularly prominent on erection. This makes coitus difficult and the probability of fertilization remote. In both these grades the scrotum is as a rule, normally developed and both testicles have usually descended.

Perineal Hypospadias. This degree is rare and represents the extreme stage of mal development. The scrotum is usually split and often one or both testes are imperfectly descended. The penis is small, retracted, and often hidden beneath a scrotal fold. In such a case, the sex may at first be indeterminable especially if the testes have not descended and it is in this instance that the child is brought up as a female until puberty or later.

Treatment. In the minor degree there is little or no interference with function either as regards micturition or in the act of coitus but in the more severe degree of penile epispadias and in all perineal forms, the disability is great. The aim of an operation is to correct the deformity and restore function. The Edmunds-Duplay operation was done in three stages, the scar was excised until the organ was completely straightened, the skin gap was filled by utilizing flaps formed from the prepuce, and a new urethra was formed from the lax skin on the under surface of the penis.

In the McIndoe, Nove-Josserand operation, also done in stages, a new urethra was formed from a fine split-skin graft. This was introduced into a tunnel which was made by a special trocar and traversed the whole length of the penis.

These operations appear to have been largely superseded by the method evolved by Denis Browne, which is based on the principle that an epithelialised track always remains patent. This operation is done in two or three stages. The scar on the under surface of the penis is excised and the organ straightened, the resultant gap is filled either by using the prepuce or by a relaxation incision on the dorsum of the penis. Some weeks later a perineal urethrostomy is established, a length of skin which is to be buried is now marked out on the under surface of the penis; it is 0·5 cm. wide, encircles the hypospadial opening, and reaches to the glans Incisions are made on either side of this area and deepened until the corpora cavernosa are reached. Each lateral flap is dissected off its respective corpus until it can be bought across the skin to be buried. A relaxation incision is made on the dorsum of the penis, stretching its whole length and the two flaps are sutured to each other with deep interrupted nylon sutures, and superficial silk stitches. The wound is healed by the fourteenth day, when the perineal urethrostomy tube is removed and the patient usually passes urine through the new canal.

Epispadias. In this deformity, the urethra opens on the dorsum of the penis and it may be glandular, penile, or complete. In the latter degree the penis is short and broad,

strictures can be controlled with intermittent dilatation but if this is not possible or is very difficult, the author's pull-through operation should be performed. Twenty-five per cent of ruptures of the prostatic urethra complain of impotence. Whilst the cause of this may in some cases by psychological, it is probable that in many cases, it is due to a nervous or vascular involvement, at the time of the injury. Injuries of the anterior urethra which are treated by formal suture, and temporary suprapubic cystostomy are very unlikely to be followed by stricture and impotence is uncommon.

Instrumental Injuries of the Urethra. These occur when too large an instrument is forced along the canal or when one is passed carelessly. Previously the commonest cause was the passage of a lithotrite but in the last 25 years the use of the resectoscope and cold punch have been more to blame. Should such an injury occur, its effects may be diminished by early regular dilatation and if a stricture develops it should be treated as on p. 145.

Neoplasms of the Penis

Benign Growths

A simple papilloma is comparatively common as are multiple warts (condylomata acuminata) which are usually venereal in origin. Fibro-lipoma and angioma also occur but are not of much significance. A papilloma is readily destroyed by applying podophyllin 25 per cent in liquid paraffin.

Malignant Growths

These are not uncommon and the large majority are epitheliomatous.

Carcinoma of the Penis. Certain chronic conditions may be precancerous such as the erythroplasia of Queyrat, first described by Paget, and analogous to the dermatitis of the nipple which bears his name. A slow growing wart harder than the common simple papilloma may gradually increase in size and develop malignant change. An epithelioma may arise on the prepuce or glans and if on the latter is usually near the corona. It is commonest in the older age group but can occur as young as 30 years of age. It is almost unknown amongst the Jews and others who have been circumcised in infancy and quite often there is some degree of phimosis present when it occurs. There are two clinical varieties—(*a*) ulcerating and (*b*) papillary. The *ulcer* is indolent with rolled edges and indurated base and in the early stages is painless If untreated it gradually spreads, destroying the prepuce, glans and body of the penis, and penetrating the urethra which leads to the formation of one or more fistulæ. If phimosis has been marked, an acute balanitis may develop and the pain and swelling which make the patient seek advice. It is then usually necessary to perform a dorsal slit of the prepuce and when this is done the ulcer is revealed. The *papillary epithelioma* usually grows very slowly and may be present for several years before the patient presents for treatment. Eventually, part of it ulcerates and will not heal From then on spread may be much more rapid. When untreated, apart from local destruction, an epithelioma of the penis spreads along the lymphatics to reach the inguinal lymph nodes. Sometimes the tumour may be on one side of the penis only but as a rule, by the time lymphatic spread has occurred, the neoplasm has more or less encircled the organ The differential diagnosis must be made from other ulcerative conditions of the penis, soft and hard chancre, erosive balanitis and infected herpes, and also from condylomata acuminata.

Treatment. As elsewhere in the body, an epithelioma may be treated by surgical

and when this occurs it may interfere with the immediate treatment and subsequent prognosis. The injury occurs when the pubo-prostatic ligaments are torn and one pubic bone is forced away from the other in this region. There is often considerable backward displacement of the prostate and this may be for as much as an inch. These injuries occur especially in high-speed road traffic accidents, and in flying accidents.

Signs and Symptoms. As a result of the concomitant injuries, the patient is usually profoundly shocked when first seen. There is the usual evidence of a fractured pelvis and even when this is uncomplicated, there is often lower abdominal pain with tenderness and guarding on palpation. If there has been an injury to the urethra as well however, there is almost always a little blood at the external urinary meatus and when this is observed rupture of the urethra is fairly certain.

Treatment. After resuscitation which may entail several hours of treatment, the urethral injury takes priority. If unfit for a major procedure, an attempt is made to introduce a catheter along the urethra. If this fails, which is usual, a suprapubic tube must be introduced into the bladder as soon as possible and if need be, under local anæsthetic. Once this has been done, definitive treatment can be postponed if necessary for 48 hours. As soon as possible however, the urethra should be realigned. This usually requires retrograde instrumentation and it may be helpful to expose the prostatic urethra retropubically. A Foley catheter with a 5 c.c. balloon is passed into the bladder, the apex of the prostate is brought forward, is stitched to the triangular ligament, and the bladder is drained. The outer end of the Foley catheter is spigotted and traction is made on it to pull on the prostate and keep the realigned urethra on stretch. This can be done by strapping the catheter to the thigh and traction should be maintained so that the Foley catheter acts as a splint. The suprapubic drain is removed in 14 days and another catheter is placed in the urethra to help the bladder wound to close.

(2) Extra-pelvic Rupture. This usually occurs in the bulbous part of the urethra. Traditionally, it has been said to occur when the metal cover of a manhole is stepped on, twists up and hits the perineum. I have seen one such case but in the majority of instances it occurs from falling astride a blunt object. The diagnosis is usually fairly easy. Together with the history of the injury there is bruising and swelling on the perineum and blood at the external meatus The rupture may be complete or only partly across the urethra.

Treatment. An attempt is made to pass a soft rubber catheter along the urethra. If successful, which is more often the case than in an intra-pelvic rupture, the catheter is left in position for 48 hours, and subsequently the patient is followed up in case a stricture should develop. If a catheter cannot be passed, an incision is made in the perineum over the swelling. The latter is usually due to blood clot which is evacuated Several bleeding vessels are then seen, picked up, and occluded. A sound is passed along the urethra when the rupture is easily identified, nor is it often difficult to find the proximal torn end. The edges are trimmed and sutured together over a rubber catheter which is then removed. The bladder is drained suprapubically for 14 days At the end of this time, the suprapubic tube is removed, a catheter is passed along the urethra into the bladder, and left in until the bladder wound is healed.

Prognosis. A considerable percentage of ruptures of the prostatic urethra develop a stricture and this is especially likely to occur when a length of the membranous urethra has been pulled up as the prostate is avulsed from the triangular ligament. Many of these



FIG 48 Filling defect on urethrogram from carcinoma of urethra



FIG. 49 Urethrogram showing extravasation in carcinoma of urethra

extirpation or irradiation. In the early stages a partial amputation of the organ should suffice. If there has been extensive spread, a radical amputation together with block dissection of the inguinal glands, is the only treatment likely to irradicate the disease.

Other Malignant Growths. Fibro-sarcoma, malignant melanoma, and endothelioma have all occasionally been reported. Most of them are highly malignant, and with the exception of fibro-sarcoma, metastasize early and tend to recur.

Neoplasms of the Urethra

Male. All tumours of the male urethra are rare. They may be benign or malignant and may occur in the anterior or posterior part.

Benign Growths

Posterior Urethra. Fibroma, adenoma, or angioma have each been reported, have usually been discovered on routine endoscopy, and are rarely of clinical significance. A simple villus papilloma can occur in the posterior urethra. It is rare, except in association with villus papilloma of the bladder and only then after the case has undergone treatment by cysto-diathermy. Polyps or œdematous tags of mucous membrane are not infrequently seen in association with chronic infection of the prostate and posterior urethra.

Anterior Urethra. Papillomata occasionally occur in the anterior urethra but are almost confined to the distal 1–2 cm. and especially just in from the external urinary meatus. They are then probably venereal in origin. They can readily be destroyed with podophyllin.

Malignant Growths

Posterior Urethra. A malignant growth is exceptionally rare, as a primary condition in this region but may spread from the bladder, from the prostate, or from the rectum.

Anterior Urethra. Carcinoma is not at all common but relatively more so here when compared with the posterior urethra. It usually occurs after middle age and may be transitional cell, columnar cell, or squamous cell. More than half the cases have had a long standing stricture of the urethra and this may mask the diagnosis. Spread to the inguinal lymph glands occurs quite early and indeed a swelling in the groin may suggest the diagnosis.

Signs and Symptoms. Increasing difficulty in passing water is the commonest symptom and the patient may at first be thought to have a stricture. He may perhaps have been under treatment for a stricture for many years and it is noticed that it ceases to respond to dilatation and bleeding readily occurs with the passage of an instrument. In such a case the early diagnosis may be difficult and is usually delayed too long for curative treatment to be applicable When the tumour arises in a previously normal urethra the prognosis is rather better. Urethroscopy may be helpful, but such an examination may be difficult or impossible on account of bleeding A urethrogram may be suggestive especially if it shows an irregular filling defect (*see* Fig. 48), but the diagnosis is often only established after biopsy The commonest site of the tumour is in the bulbous urethra and in the later stages there is then a swelling in the perineum. Should the tumour occur in the penile urethra a swelling on the shaft of the penis may be discovered fairly early. Later there is local œdema and enlarged, hard inguinal lymph glands.

produce difficulty in micturition. Further up the urethra, congenital stricture is uncommon. It is usually formed of a fold of mucous membrane and when this is so, full dilatation with division of the stricture should effect a cure. It may be accompanied by a diverticulum of the bladder.

Traumatic Stricture. This may follow rupture of the urethra, consequent upon a severe pelvic injury and is then intra-pelvic, or a blow on the perineum when it is extra-pelvic. It may follow the passage of an instrument along the urethra. In the past, this was most often a lithotrite. Now, it more often follows the use of a resectoscope or cold punch. Any instrument however, may produce this serious lesion if it is too big for the canal or if passed carelessly. The narrowest part of the urethra is the external urinary meatus and it is reasonable to expect that if an instrument can be passed through this it can pass along the remainder of the urethra without damage. When the meatus is narrow and it is essential that an endoscopic instrument should be passed, a meatotomy or a perineal urethrotomy should be performed. Stricture may follow an indwelling catheter and this does not appear to bear any relation to the length of time the catheter has remained in the urethra. It more often forms at the fossa navicularis and is very painful to dilate. Stricture has followed intra-urethral irrigation of a corrosive solution as is sometimes done by the untrained and apprehensive after exposure to venereal disease.

Inflammatory Stricture. This follows urethritis. Prior to the specific treatment of gonorrhœa, it was a common complication of this disease and may still occur when treatment is incorrect or inadequate. It is less common after non-specific urethritis and if it does occur the occlusion is not nearly so great as after gonorrhœa It rarely occurs as the result of tuberculosis and of bilharzia. The stricture forms within a few months of the infection but several years may elapse before it gives rise to sufficient disability to require treatment. A post-gonococcal stricture only occurs in the anterior urethra and then usually in the bulbous part. The scarring in the urethra is rarely confined to a small area but usually affects several centimetres. There may however, be only one narrow part or there may be several when the stricture is usually spiral. In such a case, the narrowest opening is nearly always that most posterior. The mucous membrane in the region of the stricture has been destroyed and replaced with fibrous tissue; there is also fibrosis of the submucous and muscular layers. The fibrous tissue contracts and it is this which causes narrowing and partial obliteration of the lumen. Since this contraction does not occur symmetrically, the opening is usually eccentric and is more often towards the roof than the floor of the canal.

Complications. As the result of continued obstruction, trabeculation of the bladder occurs; sometimes a diverticulum forms and then usually it is small and often multiple and in this way differs from the large diverticulum found more commonly in association with muscle bar obstruction. A similar single large diverticulum can occur in association with a congenital stricture. It is unusual for chronic retention to follow inflammatory stricture of the urethra, but it may occur. It is also unusual for a patient with a stricture of the urethra which has been treated by intermittent dilatation, to develop a simple senile enlargement of the prostate. It is not unusual in such a case, however, for a fibrosis to occur at the bladder neck and lead to the acquired form of bladder neck obstruction. It is probable that prostatic stones frequently form in association with a stricture of the urethra, and this of course may be due to the original infective process which also leads

Treatment. If the lesion is in the distal end of the urethra, partial amputation occasionally is sufficient. The lesion, however, is more often in the bulb. Radical amputation and dissection of inguinal glands may produce a satisfactory outcome but the prognosis as a whole is very grave. In the inoperable case, with retention, a suprapubic cystostomy is necessary.

Female. With the exception of caruncle, tumours of the female urethra are as rare as in the male.

Caruncle

This is a swelling, bright red in colour and varying in size but often about the size of a pea, which appears at the posterior commissure of the external urinary meatus. It is more often found in the middle aged and elderly than in the younger age group. The tumour is usually sessile but may become extruded when it becomes rather pedunculated.

The symptoms of this condition vary considerably. There may be none or it may be accompanied by much dysuria, frequency, and occasionally hæmaturia. Sometimes there may be pruritus vulvæ. The necessity for treatment depends on the severity of symptoms. If the latter are considerable, the caruncle should be removed and this is best done by diathermy. Caruncle is to be distinguished from urethral prolapse, which not only occurs in old age but also in infancy and childhood. The mucous membrane prolapses through the external urinary meatus and at first appears as a purple œdematous mass. Should it become strangulated, gangrene will set in. In the early stages, a prolapse can be replaced and the application of diathermy with a needle may produce enough scarring to prevent recurrence.

Malignant Tumours

The majority of these are carcinomatous although a sarcoma has occasionally been described. Growth is usually insidious and may spread into the peri-urethral tissue before being noticed. Usually spread has occurred to the external urinary meatus and a hard infiltrating ulcer is seen there.

Treatment. Local removal may be possible in the early stage, but as a rule total extirpation of the urethra and bladder is necessary. This operation necessitates a preliminary bypass of the ureters and this is usually effected by a uretero-colic anastomosis.

Stricture of the Urethra

In the Female

Stricture of the urethra is rare in the female and is not of much clinical importance. It does not appear to follow gonococcal infection and more often there is nothing in the history to suggest a cause although it may be due to injury either obstetrical or instrumental. It is not often severe but may cause, or be associated with, a diverticulum of the urethra. It usually responds to intermittent dilatation.

In the Male

Stricture of the urethra was at one time the commonest of urological disorders under treatment and was frequently found after a gonococcal urethritis which was improperly or inadequately treated. It is rarely of congenital origin, or may be traumatic.

Congenital Stricture. Narrowing of the external urinary meatus is fairly common but not often to such a degree as to give rise to symptoms. Occasionally however, it will

often possible to see the urethra behind and if there are multiple strictures, it may be possible to see the others arranged as a white spiral disappearing in the distance. If urethroscopy cannot be performed and there is no urgency in dealing with the case, a urethrogram should be done and besides the retrograde examination one done during micturition can be most helpful. If urethroscopy or urethrography are impracticable the urethra is explored with a series of graduated bougies. Inability to pass a small instrument along the male urethra is not definite evidence of stricture. An instrument of 18 Charrière size is first employed. If this fails to pass, smaller sizes are tried until finally one is passed but to establish the diagnosis it must also be gripped by the canal.

Treatment. This will vary with whether the stricture is complicated or uncomplicated and in the latter event also on the cause and type of stricture.

(*a*) COMPLICATED STRICTURE. An acute retention due to stricture must of course be relieved. With the correct instruments and patience it should always be possible to pass a filiform bougie. The best type to use is that which forms the guide of a Phillip's catheter. Having ascertained that a No. 12 Charrière instrument will not pass, such a guide should be employed and gentle manipulation persisted in until the bougie passes into the bladder. When successful, suitable sized follow-on instruments are attached and passed in sequence until a 14 or 16 Charrière catheter can be passed, and the bladder is then emptied. If a Phillip's instrument is not available, bougies of gradually decreasing size are employed until one is passed. If success can only be obtained with a very small calibre instrument, it is wise to rest content for the time being and to tie this instrument in the urethra with string or strapping Urine will drip alongside it and this will help to dilate the canal. In 24 hours, it should be possible to introduce a larger instrument and over a period of a few days, gradually attain full dilatation of the stricture. Should the above mentioned instruments not be available or should the operator fail to pass them, the bladder must be emptied. The correct treatment is probably an external urethrotomy but this may be difficult and beyond the scope of the surgeon. In such a case, the bladder should be drained suprapubically either by means of a Riches' tube or by direct exposure and stab puncture with a trocar capable of taking a 24 Charrière Malecot tube. If there is *extravasation of urine, a suprapubic cystostomy is performed. The whole of the affected* area must be adequately drained and at the same time an external urethrotomy performed. A peri-urethral abscess is drained and sometimes may require an external urethrotomy.

(*b*) UNCOMPLICATED STRICTURE

(i) *Of the Anterior Urethra.* The treatment will vary with the cause and position of the obstruction. A congenital stricture of the anterior urethra is usually due to a fold of mucous membrane. This may be destroyed by full dilatation and is unlikely to recur. If a stricture of the anterior urethra affects only a short segment and the remainder of the canal is normal, the stricture should be excised after the manner of Marion or Hamilton Russell. In Marion's method which is the better, after reconstitution of the canal, the bladder is drained suprapubically for 14 days. In Hamilton Russell's method, only the roof of the urethra is joined and drainage is through a urethrostomy tube for 10 days. Traumatic stricture of the anterior urethra can be treated by either of these methods but it is very unusual to find a post-gonococcal stricture which does not affect too long a segment. In such a case, the generally accepted line of treatment is dilatation. The stricture is fully dilated and is kept open by the passage of instruments at intervals. In many cases, this can be affected comparatively easy. Until full dilatation is achieved, the

to the stricture. Associated with the latter, there is frequently a persistent low grade infection which is then always secondary and not gonococcal. There may be a mild urethritis with a little discharge first thing in the morning, but more commonly this only produces some threads in the urine. Acute retention may develop either before or when undergoing treatment. A peri-urethral cellulitis or abscess may form and this may burst externally leading to fistula formation. The openings are then often multiple and give rise to the so-called "watering can" perineum. An acute epididymo-orchitis may occur spontaneously or it may follow an instrumentation. A neoplasm rarely occurs at the site of stricture and when the case is already undergoing treatment by intermittent dilatations, delay then almost always occurs in arriving at the diagnosis.

Extravasation of urine was formerly a fairly common complication. It may occur spontaneously if the urethra ruptures proximal to the stricture, or it may be produced by inaccurate instrumentation. It can occur at the first and subsequent urinations after rupture of the urethra. It involves the anterior part of the perineum, the scrotum, penis, and anterior abdominal wall but does not pass behind the posterior margin of the triangular ligament or further down the thigh than 4 cm. below the inguinal ligament on account of the arrangement of the superficial fascia. Except in traumatic rupture the urine is usually infected but in itself urine is lethal to soft tissues and the affected part rapidly swells, becomes tense, and fluctuant. A large area of the subcutaneous tissue and skin becomes gangrenous and beneath this very offensive pus and urine are mixed.

Signs and Symptoms. These will depend on the narrowness of the lumen and on the presence of one or more complications. The patients' most common complaint is of increasing difficulty in micturition. At first the stream is diminished in size although not so much in force, but the calibre of the opening becomes narrower until ultimately the stream comes out in driblets. Acute retention may then develop and usually remains complete; only very rarely does overflow occur when it may go on to become a chronic retention. Neither the shape of the stream nor its direction are affected by a stricture in the bulb, but if the obstruction is in the distal urethra the jet may be bifid or corkscrew. There is no alteration in the frequency of the act with an uncomplicated stricture but an accompanying cystitis may alter this.

If extravasation of urine should occur there is a sudden pain in the perineum and swelling quickly takes place The swelling is at first red but areas of blue discoloration from gangrene are soon apparent. The local area is acutely tender and fluctuation can be elicited quite early. Generally, the patient rapidly becomes quite ill with a swinging temperature, dirty furred tongue, and ammoniacal breath He is toxic and appears pale, is dehydrated, and shrunken around the eyes.

Diagnosis. In uncomplicated stricture, the diagnosis is established by anterior urethroscopy or by urethrogram and is suggested when a bougie, smaller that the external meatus, is partially obstructed and gripped in the canal. Urethroscopy should always be attempted except when there is acute retention and it can only be done if a cannula can be passed along the urethra It is very unlikely that such a cannula can be passed through the opening of a stricture. At this examination, if a wide stricture is present, a ridge is seen which runs round the wall and which stands out white from the rest of the mucous membrane. A narrower stricture appears like a white diaphragm across the lumen of the urethra, and the opening which is usually eccentric can be seen as a black recess varying in size down to that of a pin head. When the stricture is of moderate sized calibre it is

almost confined to epithelioma. This is an occupational disease, known as chimney-sweep or mule spinner's (textile workers) cancer, but it may occur in any industry where men are exposed to long continued soiling from tar, pitch, or mineral oils The lesion starts as a flat wart, which at first slowly increases in size and ultimately ulcerates. The ulcer does not heal, has hard indurated and everted edges, and gradually extends. The inguinal lymph nodes become affected early on. The condition has become much less common since the cause was recognized and, by suitable precaution, exposure largely eliminated.

Treatment. Radical excision together with dissection of the inguinal and femoral glands is the most effective treatment.

INFECTIONS

Infections of the scrotum are similar to those affecting the skin elsewhere. Gangrene occurs in extravasation of urine, but apart from this a condition of spontaneous gangrene has very occasionally been seen. This is probably due to infection from Bacteroides melano-genicium.

patient is seen weekly and then the time between treatments is extended until the optimum interval is reached. This is indicated if a suitable sized instrument can be passed without difficulty and may be as long as 12 months. In such a case the stricture may well be cured. More often the interval between is 3-6 months and in resistant cases may be as short as once a fortnight. Not all cases are suitable to treat in this way. If there are several strictures the openings of which are out of line, the passage of the first instrument may be extremely difficult at each treatment and the same can apply if a false passage has been made. Such a case can be dealt with by using a Phillip's guide and follow-on bougies, it may be helped by an internal urethrotomy by a period of continuous dilatation and in the very difficult case may require an external urethrotomy. It is for this type of case that various operative procedures have been employed and the Denis Browne technique has been applied by Bengt Johanson, Sweeny, and others. Rarely the greater part of the anterior urethra has become completely occluded. It may then be that the alternative to a suprapubic cystostomy is a permanent perineal urethrostomy.

(ii) *Of the Posterior Urethra.* Intra-pelvic rupture is difficult to treat satisfactorily and results in stricture in a number of cases. Many of these can be treated by intermittent dilatation but in certain cases this is not so. Instrumentation may be extremely difficult and may invariably be followed by retention of urine. The urethra may be impassable and if it is also impermeable a suprapubic fistula is present. In such a case, the author's pull-through operation should be employed and will usually give a satisfactory result. This operation is only suitable for a patient with a functioning internal sphincter and should be reserved for stricture of the prostatic urethra or for one of the anterior urethra which is so near the triangular ligament that it cannot be excised.

DISEASES OF THE SCROTUM

Many conditions which affect the scrotum occur elsewhere on the integument of the body but one or two are peculiar to this region.

Elephantiasis

Enormous hypertrophy of the scrotum from elephantiasis occurs mainly in tropical and subtropical countries It is due to blockage of the lymphatic ducts by the filarial form of a nematode and is spread by the mosquito. Repeated attacks of lymphangitis occur and with each attack the scrotum becomes larger and larger. There is little else in the way of symptoms and the main disability is from the great swelling of the scrotum.

Treatment. Apart from excision of the scrotal mass little can be done.

Lymph œdema of the scrotum may occasionally occur with blockage of the pelvic lymphatics from other causes such as malignant disease. Thrombosis in part or in the whole of the vesico-prostatic plexus may give an œdema which is localized to the penis and scrotum and which pits on pressure.

Neoplasms of the Scrotum

Benign tumours of the scrotum are quite common. Cystadenomata may be present in large numbers, are usually small, and of little significance Pedunculated fibrolipomata which may reach considerable size and become quite pendulous are fairly common and myxoma has also been described Malignant tumours of the scrotum are

bifurcation of the abdominal aorta and the iliac arteries, the internal carotid artery and the anterior or posterior tibial arteries.

Thrombosis of the Abdominal Aorta. (Allbutt and Rolleston, 1909, Leriche, 1923.) This lesion often produces surprisingly mild symptoms and is by no means uncommon. The symptoms include intermittent claudication, sexual impotence in the male, and



FIG 50 Thrombosis of the terminal aorta in a patient aged 39. The onset of symptoms was gradual and when this aortogram was taken the patient could still walk for a quarter of a mile before the onset of pain

occasionally rest pain or gangrene. A few patients with occlusions as high as the renal arteries suffer from hypertension with severe headaches; and anuria may follow if the renal arteries become closed. It is of importance to realize that this lesion may be confused with a lumbar disc lesion and no less than 3 of our 73 patients had a lumbar disc operation before a correct diagnosis was made and they were referred to us. The diagnosis is made by finding absent or weak femoral pulses in a patient without evidence of coarctation of the aorta and confirmed by aortography which also serves to show the extent of the disease.

From the practical point of view, thrombosis of the abdominal aorta may be divided into three types: those with a *thrombosis moderately well-localized to the*

CHAPTER II

PERIPHERAL VASCULAR DISEASES

CHARLES ROB

DISEASES OF ARTERIES

Chronic Arterial Occlusion

Atherosclerosis

THIS disease is the commonest cause of death and a frequent cause of disability. As we grow older our arteries degenerate. In some this takes the form of degeneration of the medial coat which either calcifies, when few if any symptoms develop, or the artery may dilate and an aneurysm form; for the majority this degeneration takes the form of atheromatous plaques on the intima—these rarely cause the patient any inconvenience until the artery thromboses. Contrary to what is often taught, an artery may have advanced atheromatous lesions and yet it is unusual, with the possible exception of the coronary arteries, for the patient to notice any abnormality until the vessel has thrombosed or nearly so. The terminology connected with this disease has become confused. Most authorities today consider that arteriosclerosis refers to the degenerative lesions of the medial coat, that atheroma is the correct term for the plaques of lipid material which form in the intima and that, because the two lesions may develop separately or together, atherosclerosis should be a term reserved for the disease when both forms are present in the same patient. It is also important to stress that many consider atheroma to be a disease and possibly a preventable disease, particularly by control of diet, whilst arteriosclerosis is an inevitable accompaniment to ageing. Whilst the cause of atheroma is not known, there is considerable evidence that it is commoner in those who have an abnormality of their lipid metabolism, who take a diet with a high content of animal fats [Bronte Stewart, Antonis, Eales, and Brock (1956), Oliver and Boyd (1956)], who smoke cigarettes excessively, who are diabetic, who take little muscular exercise, and who work hard without adequate periods of relaxation It is possible that repeated minor local trauma may account for the frequent occurrence of this disease in such sites as the femoro-popliteal junction where the artery passes through the adductor hiatus, but it is difficult to explain the by no means uncommon occlusion which occurs at the bifurcation of the abdominal aorta in this way. Patients of both sexes suffer from atherosclerosis but it is commoner in men and in women after the menopause and, whilst it may occur before the age of 20, it is uncommon for symptoms to develop before the age of 35, but in our experience it is the commonest cause of the symptom of intermittent claudication in patients of this age and after. The abnormal level of certain blood lipids in some of these patients may produce effects in one or both of two ways, either the lipid may settle in the subintimal layer and produce plaques of atheroma or it may aggravate the tendency to intravascular thrombosis found in atheromatous arteries.

Any artery in the body can be affected by atherosclerosis, the most frequent sites for thrombosis being the femoral-popliteal artery, the coronary or cerebral arteries, the

terminal aorta and iliac arteries (Fig. 50), those with a high occlusion level with the origin of the left renal artery (Figs. 51 and 52) and those with an unusually well-localized lesion (Fig. 53).

Thrombosis of the Iliac Arteries. This often occurs in patients with a relatively normal aorta. The disease may spread later to involve the terminal aorta and iliac vessels on the opposite side. The first vessel to thrombose may be the common, external or internal iliac artery. If it is the internal iliac artery then the patient will suffer from intermittent



FIG 53 A well-localized occlusion of the right common iliac artery. The patient was unable to work and developed intermittent claudication of the calf muscles after walking 50 yards.

claudication of the gluteal muscles and clinical examination will show a normal femoral pulse on that side. Occlusion of the common iliac artery produces similar claudication in the buttock but, in addition, the femoral pulse will be weak or impalpable and the claudication pain may also be felt in the calf of the leg or thigh, whilst a patient with an external iliac occlusion suffers from intermittent claudication in the calf and thigh only. Figs 53 and 54 are arteriograms from a general labourer aged 48 who had a well-localized occlusion of the common iliac artery, an ideal case for the operation of thrombo-endarterectomy as shown in Fig. 54, a post-operative arteriogram.

Occlusion of these vessels and of the aorta may lead to gangrene of the toes. Fortunately many of such patients can avoid a major amputation if an efficient arterial reconstruction operation is performed (Rob, 1957). Figs. 55 (*a*) and (*b*) illustrate this.

Thrombosis of the Femoro-Popliteal Arteries. This, the commonest thrombosis of a peripheral artery, produces intermittent claudication and sometimes rest pain or gangrene. The common femoral pulse is palpable but, except in an occasional patient with a

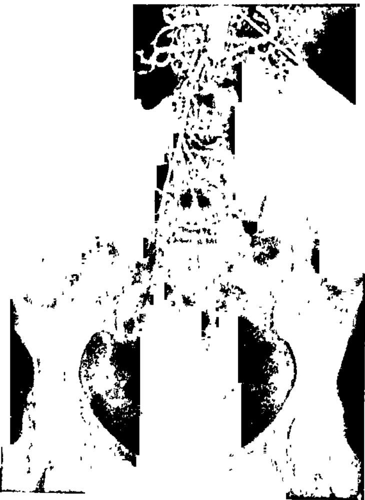


FIG. 51. A high occlusion of the abdominal aorta at the level of the renal arteries. The patient was hypertensive and there were casts and red blood cells in her urine.



FIG. 52. In 1952 an arterial transplant was inserted into the patient shown in Fig. 51. Five years later she was able to walk for miles, all her ankle pulses were present and her blood pressure was normal.



(a)



(b)

FIG 55(a) (b) [illegible]

localized occlusion and an unusually well-developed collateral circulation, all pulses distal to this are absent, and in this latter type of patient the ankle pulses disappear with exercise. In cases of doubt an oscillometer applied to the calf of the leg helps to localize the level of the arterial occlusion.

Thrombosis of the Arteries of the Leg or Foot. The arteries of the calf of the leg may thrombose individually or the occlusion may occur in conjunction with a thrombosis of



FIG 54 The patient shown in Fig 53 after the operation of thrombo-endarterectomy He now does a full day's work as a general labourer.

the femoral or popliteal arteries, in which case gangrene is more likely to follow (Mavor, 1957). In the foot a by no means unusual occlusion is of the planter arch and sometimes of the digital arteries. These patients have palpable ankle pulses and gangrene or threatened gangrene of the forefoot, they do very well after a transmetatarsal amputation if gangrene makes that necessary.

Thrombosis of the Arteries of the Upper Limb. In our experience the commonest *artery in the upper limb to thrombose is a digital artery, but any vessel may become* occluded, particularly in those who use crutches or subject their limbs to excessive strain (Rob and Standevan, 1956). In the upper limb, however, atherosclerosis is less common than thromboangiitis obliterans as a cause of obliterative arterial disease in men.

Thrombosis of the Small Vessels of the Hands and Feet. Whilst the most common cause for occlusion of these vessels is not atherosclerosis but thromboangiitis obliterans, it is by no means uncommon in patients with this disease. The clinical picture is one of local ischæmia with normal ankle or wrist pulses. If the digital arteries thrombose then

eventually lost both feet, one hand, and four fingers from the other hand. It is very rare for the disease to develop in a patient over 40 years of age and even at the age of 35 years atherosclerosis is a more common cause of ischæmic symptoms in a limb.

The first clinical abnormalities arise when an artery or vein thromboses. After this the disease if untreated is progressive but episodic. If the first vessel to thrombose is an artery then the symptoms are either of intermittent claudication, paræsthesiae, coldness, numbness, rest pain, or gangrene. If a vein, then the patient notices a painful tender lump as it is usually a superficial vein which becomes occluded. It is probable that thromboangiitis obliterans is the commonest cause of the clinical condition known as thrombophlebitis migrans.

The arterial occlusions are usually of small peripheral vessels but later vessels of the size of the posterior tibial or dorsalis pedis become involved (Fig. 57) with spread eventually to the main popliteal or femoral artery.



FIG 57. The typical arteriogram of thromboangiitis obliterans Note the occlusion of the arteries of the leg

Primary Thrombosis

This uncommon lesion may follow a closed injury but sometimes occurs without any obvious cause. The patient, a young adult, presents with the clinical features of an arterial thrombosis usually of the popliteal artery. An essential point for the confirmation of the diagnosis is that the patient should have no evidence of atherosclerosis because this is a very common cause of an arterial thrombosis, whilst a primary thrombosis is a rarity.

Investigation of a Patient with Chronic Arterial Occlusion

As stated, careful palpation of the arterial pulse at the groin, popliteal fossa and ankle or in the upper limb is the main diagnostic test and in nearly every patient this simple procedure serves to make a diagnosis of the site of the arterial occlusion. Examination with an oscillometer or an arteriogram merely serves to confirm this clinical impression. It is important, however, to examine the whole patient and to obtain a good family history because atherosclerosis is a general disease and therefore such tests as an electrocardiogram and examination of the state of the retinal vessels with an ophthalmoscope are of importance A possible

one or more fingers or toes will be ischæmic and perhaps gangrenous, but if, as sometimes happens, the occlusion is in the plantar arch the whole forefoot is in danger. The importance of these lesions is that local amputations are followed by good healing.

Thrombosis of Other Arteries. Any artery in the body may thrombose in a patient with atherosclerosis. Of those not yet mentioned the coronary and cerebral vessels are of great importance but of particular interest to the surgeon are the mesenteric, internal carotid and renal arteries. The surgery of mesenteric occlusion has been discussed in the



FIG. 56 Aortogram showing partial occlusion of the left renal artery in a patient with severe hypertension 220/160 Reconstruction of the thrombosed aorta and removal of his left kidney reduced the blood pressure to 140/80

first volume, but it is important to realize that some patients with the syndrome of internal carotid thrombosis can occasionally be cured by an arterial reconstruction operation (Eastcott, Pickering, and Rob, 1954) and that some patients with severe arterial hypertension have a partial thrombosis of one renal artery (Fig. 56) (Rob, 1956).

Thromboangiitis Obliterans

Buerger's Disease (Buerger, 1928) As the name implies, this is an inflammatory lesion of arteries and veins which causes them to thrombose. The cause is not known but there is conclusive evidence that tobacco smoking is a factor which aggravates this disease. All patients who have this disease should abandon smoking completely, immediately, and permanently. This disease is almost unknown in women; we have only seen one example in a woman and she was a chain smoker who refused to stop and

administration of various drugs or gases such as oxygen, physiotherapy, and care of the feet to minimize the risk of infection and of minor traumata, as for example in cutting the nails, the avoidance of excessive heat to parts which are already ischæmic, reduction of body weight if this is excessive and a careful explanation of the nature of the disease to the patient.

Surgical Treatment. (*See* pages 160–61.) A variety of operations have been used for the treatment of patients with chronic arterial occlusion. These include sympathetic ganglionectomy or phenol sympathetic block (Haxton, 1947), adrenalectomy, thrombo-endarterectomy, an arterial transplant or other form of arterial reconstruction, Achilles tenotomy, popliteal neurectomy, the creation of an arterio-venous fistula between the femoral vessels and the various amputations. The details of some of these procedures will be discussed later but in patients with rest pain or gangrene the ideal to aim at is an arterial reconstruction operation and, in our view, an amputation can be avoided in about 20 per cent of such patients by this operation (Rob, 1957). If a reconstruction procedure is not possible then a sympathetic ganglionectomy may delay amputation in some early cases and enable the surgeon to amputate at a lower level in other patients. Apart from this, both sympathetic ganglionectomy and arterial reconstruction operations have a place in the management of patients with intermittent claudication but here selection should be strict (Rob, 1953, Rob, 1956). Adrenalectomy is widely used in many centres, particularly in France, for the treatment of patients with thromboangiitis obliterans. There is considerable evidence that patients with this disease do have adrenal hyper-activity but we have as yet little experience of this operation for this disease. Popliteal neurectomy and the creation of a femoral arterio-venous fistula are procedures which are not used today. On the other hand, Achilles tenotomy is a minor procedure of value in those with patients who have severe intermittent claudication of the calf muscles. A patient with a claudication distance of about 50 yards is able to walk better after this procedure but for those who can walk for about 100 yards before the onset of pain the disability of a divided Achilles tendon about equals that of the arterial insufficiency.

Acute Arterial Occlusion. Embolism. Thrombosis. Injury

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Clinical Picture

A patient with sudden occlusion of a major peripheral artery calls in his doctor because the limb has become cold, pale, and perhaps numb, because agonizing pain has developed at rest, or because of the sudden onset of severe intermittent claudication. The severity of the symptoms varies with the rate of occlusion of the vessel, which means that they are usually more pronounced when the vessel has been blocked by an embolus than

precipitating cause such as diabetes must be looked for in every case and where facilities exist the blood lipids should be estimated, particularly the β lipoproteins.

In the past much time has been spent on performing the various sympathetic release tests in patients with chronic obliterative arterial disease to try to discover which patients will benefit from a sympathetic ganglionectomy. Unfortunately these tests, whilst possibly having a place in the investigation of patients with vasospastic diseases such as Raynaud's phenomenon, have no place in the investigation of those with atherosclerosis because the results of the test bear no relation to the clinical response to sympathetic ganglionectomy.

Other tests such as an estimation of the venous filling time, the colour changes with posture, the reactive hyperæmia test, skin temperature estimations, and plethysmography show the degree of ischæmia, but this can be estimated with equal efficiency by a simple clinical examination and a careful history. However, they should be used by all who are studying these diseases, as opposed to performing clinical tests alone, as may also other investigation techniques such as capillary microscopy and the use of radioactive isotopes to study the rate of blood flow.

Treatment of Chronic Arterial Occlusion

The first essential is to treat the cause. In the case of atherosclerosis this is difficult but there is some evidence that long-term anticoagulant therapy may reduce the incidence of further thromboses, that a diet low in animal fats may limit the formation of atheromatous plaques and, of course, if the patient is a diabetic this should be controlled.

For long-term anticoagulant therapy we use Dindevan (phenylindanedione) in sufficient dosage to double the patient's prothrombin time and to keep it at a level just less than this for years or even for the rest of the patient's life. For example, a patient whose prothrombin time is 15 seconds should have it raised to about 28 seconds, which can be achieved in most patients with a dosage of Dindevan of between 50 and 200 mgm per day *in divided doses. Careful control is required and the prothrombin time* should be estimated every second day at first and then at weekly and later monthly intervals when the level has become stable. The antidote to Dindevan is Vitamin K_1 2 ml. and this should be taken if the patient suffers from a hæmorrhagic episode but it is unnecessary to stop anticoagulant therapy of this type for such procedures as a surgical operation and some recommend it as a precaution before and during the operation of mitral valvotomy. This requires some explanation as to why the treatment is effective if hæmorrhage during surgery is apparently normal. The reason is that Dindevan depresses the production of factors 5 and 7, this delays the clotting time of the blood but makes little difference to the bleeding when control has been efficient. A state of affairs which does not occur when heparin which is an antithrombin, is used as the anticoagulant. This latter fact is of some importance because there is some evidence that the sudden stopping of anticoagulants in a patient who has taken them for a long time may be followed by a further arterial thrombosis

Patients who are suffering from thromboangiitis obliterans may also benefit from long-term anticoagulant therapy but here it is vital that the patient should stop smoking immediately, completely, and permanently.

Other medical measures include vasodilator drugs such as Priscol or dibenyline, but these are of little help unless the peripheral arteries only are occluded, the intra-arterial

administration of various drugs or gases such as oxygen, physiotherapy, and care of the feet to minimize the risk of infection and of minor traumata, as for example in cutting the nails, the avoidance of excessive heat to parts which are already ischæmic, reduction of body weight if this is excessive and a careful explanation of the nature of the disease to the patient.

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when it thromboses. There may be a previous history of intermittent claudication, a stroke, or angina pectoris, pointing to an arterial thrombosis as the reason for the new symptoms; or the patient may be suffering from auricular fibrillation or bacterial endocarditis, indicating that an embolus is the likely cause.

Pain is said to be a marked feature of an arterial embolus and usually absent when the blood flow has been interrupted by a thrombosis or an injury. This is on the whole true, but some patients develop no pain after an undoubted arterial embolus and others suffer *agonizing pain from a thrombosis. Later the limb becomes numb and, if gangrene is* likely, the muscles can no longer contract and ischæmia of the nerve fibres leads to complete sensory and motor paralysis; in other patients gangrene is averted but severe rest pain develops.

The limb at first is pale and cold; in a severe case the skin looks and feels dead. Later the skin becomes cyanosed and, if gangrene is certain, a dark purple colour; usually areas of pallor are adjacent to areas of cyanosis, giving the skin a blotchy appearance. The temperature of the environment is of great importance both to the rate of onset of the various clinical signs and to the chances of recovery. If the part is kept cool, skin can withstand severe anorexia for 48 hours or more, muscle for 10 hours or so; nerve conduction ceases after about 30 minutes. Recovery from complete anoxia is much more likely after restoration of the blood flow if the part has been cooled. On the other hand, if the part has been warmed, blisters may form on the skin within 12 hours and muscle becomes gangrenous within a few hours.

The pulses are absent distal to the lesion and increased proximally. Thus a patient with a popliteal embolus will have no palpable pulsation in either the dorsalis pedis or posterior tibial arteries, but the popliteal artery will be unduly prominent because the embolus usually rests on the bifurcation of an artery and the main vessel above appears to pulsate more forcibly than on the normal side.

Treatment

There can be few emergencies which are influenced to a greater extent by good initial *medical care than sudden occlusion of the main artery to a limb. Whilst admission to* hospital should be obtained if possible, the first few hours are of great importance. Incurable changes can occur during this time. Simple measures taken in the patient's own home serve to minimize the effects of such a lesion. Unfortunately there can be no doubt that many patients with sudden arterial occlusion do not receive the best treatment. In particular, heating the limb by blankets or hot-water bottles does much harm. *It can be stated that a patient who receives no treatment at all is better off than one whose* limb has been either heated or elevated.

Treatment is discussed under the following headings: the reduction of the metabolic needs of the part; development of the collateral circulation; anticoagulants; maintenance of the patient's general health and the prevention of infection and deformity; and surgical operations.

Reduction of the Metabolic Needs. This is best achieved by keeping the limb cool. It should be exposed to the air at room temperature in temperate or cool climates or cooled by a fan in the Tropics. Cooling reduces cell metabolism and less oxygen is required, so that the part has a better chance of surviving until the blood flow is restored. Rest further reduces the metabolic needs; therefore active movements of the affected

limb should be avoided and if necessary a light and well-padded splint applied. Rest may also be encouraged by the relief of pain, for which purpose pethidine, 100 to 150 mg. is usually more effective than morphine, ¼ gr. (16 mg.). For those patients with minimal pain a hypnotic such as amylobarbitone, 3 gr (0 2 g) is of value A good drug for this purpose is alcohol; this often relieves the pain of sudden vascular occlusion, probably because it is antispasmodic, and at the same time it helps the patient to sleep. One to 2 oz. (28–57 ml.) of whisky or brandy four-hourly is a satisfactory dose for these patients. It is important not to elevate the limb; the position of maximum comfort which most patients adopt in bed with the head and shoulders raised on two or three pillows and the trunk and limbs flat or slightly dependent is also the best position for an ischæmic lower limb. Some patients obtain considerable relief when the limb is dependent; in acute vascular occlusion this may be allowed, but not for long periods.

COLLATERAL CIRCULATION. The development of the collateral circulation may be encouraged in a number of ways. The most efficient and at the same time the simplest measure is to establish reflex vasodilatation. To obtain this the affected part should be cooled and the rest of the body heated. With the patient in bed the method we use is to arrange the bedclothes in such a way that the affected limb is exposed to the air. The patient's other lower limb should be covered with a thick woollen sock, and both it and the trunk covered with blankets; a long-sleeved sweater and vest should be worn over the pyjama jacket and the hands in particular should be warmed; this is most easily achieved by asking the patient to wear a pair of woollen gloves, although electrically heated gloves are better if available. In the case of sudden occlusion of a main artery to the upper limb, this limb should be cooled, and the feet, trunk, and other hand warmed.

Evidence produced by Sir Thomas Lewis and others has established that the vasodilatation produced in this way equals and possibly exceeds that of either a sympathectomy or a sympathetic nerve block. In some patients reflex vasodilatation worsens pain, but this often coincides with recovery of the circulation and is therefore a worthwhile price to pay.

It is important that splints, dressings or the patient's posture should not constrict the region of vascular occlusion around which the collateral vessels must develop. Vasodilator drugs are of value, but in my opinion no proprietary preparation is superior to alcohol as a vasodilator in patients with sudden peripheral arterial occlusion; as already stated, this should be prescribed in liberal doses. Papaverine hydrochloride, ½ to 1 gr. (32–65 mg.), given intra-arterially, proximal to the lesion, may help to promote vasodilatation. Tobacco, on the other hand, causes peripheral vasoconstriction, and a wise patient stops smoking after sudden occlusion of a peripheral artery.

Sympathetic block with procaine hydrochloride or phenol is no better than reflex vasodilatation in promoting the development of the collateral circulation, but if performed with phenol it does enable some patients who would otherwise be bedridden to resume a sedentary occupation. It has no place in the treatment of an acutely ischæmic limb, but a real place in the treatment of elderly and poor-risk patients and of those who need prolonged sympathetic denervation but do not want a surgical operation. The technique consists in placing the patient on his side with the vertebral column straight, the third lumbar vertebra is located and a long (12 cm.) needle inserted at this level, and at a distance of 7 cm. (2¾ in.) from the midline; the needle should be directed inwards and

advanced until it reaches the side of the body of the vertebra, it should then be manipulated until it slides forward to lie just in front of the convex antero-lateral surface of this bone. Aspiration serves to exclude the presence of blood or cerebro-spinal fluid, and then 4 ml. of 4 per cent procaine should be injected; if this produces a sympathetic block 10 ml. of 10 per cent phenol in water is injected and the patient told to lie still for half an hour. This type of block produces a long-lasting sympathetic denervation.

ANTICOAGULANTS. Anticoagulants have an important place in the management of patients with sudden vascular occlusion. They help to limit the extension of the thrombus, particularly into the vessel distal to the block where the blood flow is sluggish. They should be used as a routine during the acute stage in all patients with sudden occlusion of the main artery to a limb, and for long periods afterwards in certain patients with arterial thromboses. Heparin, 15,000 units, should be given at once, preferably by intravenous injection, alternatively intramuscularly, and repeated six-hourly for 18 hours. At the same time phenylindanedione, 200 mg., by mouth, should be given and repeated twice daily in doses of 100 mg. Phenylindanedione takes about 18 hours to become effective, and so this combination of drugs produces a rapid effect which can be maintained for an indefinite period by the oral route. Control is by the prothrombin time; this should be reduced to give a prothrombin level of just less than twice the patient's control prothrombin time. Most patients reach this level on a dose of 100 mg. daily in divided doses, but some require only 50 mg and others as much as 150 mg

Should an overdose of heparin be given the antidote is an intravenous injection of 10 ml. of 1 per cent protamine sulphate, and the antidote for phenylindanedione is 20 mg of vitamin K_1, given orally. The above dosages for heparin and phenylindanedione refer to patients without a recent surgical or other wound Both drugs are very difficult to control in patients with a recent wound and should only be prescribed by those with considerable experience.

GENERAL MANAGEMENT. The general health of the patient must be maintained by ensuring an adequate intake of food and adequate sleep. Infection, an ever-present danger in ischæmic tissues, is best prevented by dressing all breaches in the skin with a careful aseptic technique and prescribing penicillin, 1,000,000 units twice daily, at the slightest sign that an infection is becoming established. Deformities may occur, particularly if a Volkmann type of contracture develops in the ischæmic muscle; these may be minimized by putting all joints through a full range of passive movement once a day. In some patients the ischæmic muscles are too painful to permit this. In these cases a light splint helps to prevent the development of gross deformities, particularly that of foot-drop.

OPERATIVE TREATMENT. Surgical operations, such as embolectomy, endarterectomy, arterial repair or an arterial graft, may succeed in restoring a normal blood flow. Others—for example, sympathectomy, incisions in the deep fascia, or arterectomy—may be used to assist the development of a collateral circulation Alternatively, operation may be resorted to because conservative treatment has failed, when an amputation is necessary either for gangrene or for intolerable rest pain.

Embolectomy is rarely needed in the upper limb, the collateral circulation here is so efficient that the pulse usually returns to the wrist within 48 hours of a brachial embolus. On the other hand, embolic obstruction of the bifurcation of the abdominal aorta is best treated by immediate operation, as are many embolic obstructions of the popliteal or common femoral arteries A great deal depends upon the appearance of the limb; in

many patients the blood flow is returning by the time the patient reaches hospital, and conservative treatment with anticoagulants and reflex vasodilatation alone is effective; however, where there are good facilities popliteal or common femoral embolectomy usually pays, for by this means a normal blood flow can be restored. Arterial repair and arterial grafting have their most important indication in those patients with sudden arterial occlusion due to an injury; of obvious importance in war, these injuries when they occur in peacetime require adequate surgical treatment. For example, we have seen in the last two years three butchers who had accidentally divided their femoral arteries with their own knives; in one an end-to-end suture was possible, and in the other two an arterial graft was necessary; all now have patent vessels with a good blood flow and palpable pulses distal to the lesion.

Sympathectomy is of great value after the acute phase has passed; before this it has a place in those patients who cannot tolerate reflex vasodilatation. The object of the operation is to increase the collateral circulation around the occluded artery. In addition, sympathectomy makes the skin warm and dry—a valuable contribution to the welfare of a patient with an ischæmic limb. The other two operations designed to assist the development of the collateral circulation—arterectomy and incisions in the deep fascia—have in my view little real value.

Amputation, whilst being a last resort, should not be unduly delayed in patients with rest pain. The level varies with the level of occlusion in the arterial tree and the efficiency of the collateral circulation. With experience, many patients can receive the added benefit of a conservative operation, but in others a major above-knee amputation is required. The important thing is to obtain primary healing of the skin flaps and a stump which is useful.

Arterial Aneurysms

(Rob, 1954, De Bakey, Cooley and Creech, 1955, Rob, Eastcott, and Owen, 1956). There are six main reasons why a patient develops an arterial aneurysm. These are:

Congenital abnormalities
Trauma
Atherosclerosis.
Syphilis.
Mycotic aneurysms in patients with bacterial endocarditis.
Polyarteritis nodosa and allied diseases.

Congenital Aneurysms

Congenital aneurysms usually occur on the cerebral vessels; they are rarely seen in other parts of the body. They are symptomless until they leak or rupture, when the clinical features of an intra-cerebral or, more frequently, of a sub-arachnoid hæmorrhage develop. The diagnosis of these aneurysms has been greatly assisted by the development of efficient cerebral arteriography; once such an aneurysm has been located many of these patients can be improved by surgery.

Traumatic Aneurysms

Traumatic aneurysms are common in war and rare in peacetime. They may be caused by both closed and open injuries. Most traumatic aneurysms are false. A false aneurysm

may be defined as one in which the greater part of the wall of the sac is formed by organized blood clot supported by the tissues of the host. A true aneurysm has a sac composed of one or more coats of the artery. In the days when bleeding patients was one of a surgeon's main activities arterial aneurysms were frequently caused by this operation and it is of interest that the first arterio-venous fistula to be described occurred as a result of such an accident (Hunter, 1764).

Atherosclerosis

Atherosclerosis is a common cause of an aneurysm and now that syphilis is disappearing from Britain it is the commonest cause. Common sites are the aorta where atherosclerosis usually produces a fusiform aneurysm in the thoracic portion and a more saccular aneurysm in the abdominal aorta. The popliteal artery and the femoral just distal to the inguinal ligament are fairly frequent sites: in the latter situation the aneurysms are often bilateral. Atherosclerotic aneurysms usually present in patients over 50 years of age. They are at least ten times more common in men than in women. One manifestation of atherosclerosis is a localized destruction of the medical coats and of the elastic fibres; once this has occurred an aneurysm may develop. Local strain or injury is a possible factor in the production of both atherosclerotic and syphilitic aneurysms; an already weakened artery gives way at sites of excessive strain such as the popliteal or common femoral vessels.

Syphilis

Syphilis was a very common cause of aneurysms of the thoracic aorta and a fairly common cause of peripheral arterial aneurysms. The improved treatment of this disease by the arsenicals reduced the incidence and, now that penicillin has caused secondary signs to be a rarity, these cases are getting more and more uncommon.

Mycotic Aneurysms

Mycotic aneurysms, on the other hand, are increasing in importance, particularly to surgeons These aneurysms are usually secondary to bacterial endocarditis; before the discovery of penicillin the primary disease was nearly always fatal and the aneurysm therefore of only passing interest. Now that the endocarditis can be cured the aneurysm remains and is referred to the surgeon for treatment. The commonest site for a mycotic aneurysm is adjacent to a coarctation of the aorta, the aneurysm developing as a result of an infective process in the aortic wall. At other sites in the peripheral vessels an infected embolus either of the vessel itself or of one of the vasa vasorum is the most likely cause.

Polyarteritis Nodosa

Polyarteritis nodosa and certain allied conditions produce multiple aneurysms of small arteries. It is these aneurysms which form the nodules which originally gave the disease its name. Beyond the fact that the small aneurysms in patients with polyarteritis nodosa tend to rupture and thereby cause symptoms which may confuse a surgical diagnosis, they have little interest to the surgeon, but occasionally the larger vessels become involved These aneurysms develop in young or middle-aged patients and when seen it is important to realize that they are part of a general disease which can be controlled by cortisone. We once resected a large aneurysm of the carotid artery in a young

man, only for him to die six weeks later from a ruptured mesenteric aneurysm; at a post-mortem examination a large number of small and medium-sized aneurysms were found throughout the arteries arising from his abdominal aorta.

Aneurysms are usually divided into three types; saccular, fusiform, and dissecting. Saccular and fusiform are merely descriptive terms and, whilst these describe adequately some cases, in most patients the aneurysm is a combination of the two shapes. Fig. 58

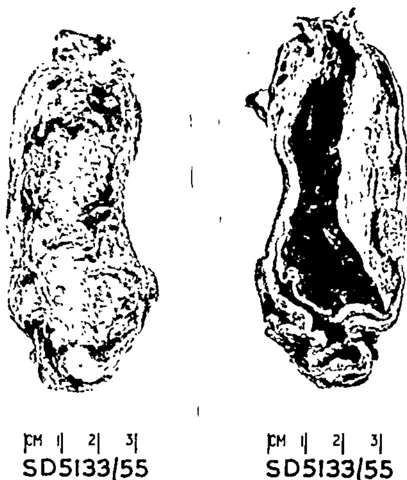


FIG 58 An aneurysm of the lower abdominal aorta and of the common iliac arteries removed at operation Note the clot in the walls Continuity was restored with a homologous arterial transplant

illustrates an abdominal aneurysm which was resected, the vessel was reconstructed with an arterial graft; this aneurysm is fusiform in its aortic portion but saccular in each of the common iliac vessels. In our experience most aneurysms of the lower abdominal aorta conform to this type and, if reconstructive surgery is contemplated, the transplant or prosthesis must include both common iliac arteries with a short length of the external and internal iliac vessels as well so that the whole area can, if necessary, be replaced.

Clinical Features. These vary with the site of the aneurysm. In this section I shall confine my remarks to aneurysms of the abdominal aorta and the peripheral arteries. I shall not discuss the numerous clinical abnormalities produced by aneurysms of the thoracic aorta or of the cerebral arteries

Most abdominal aneurysms cause pain, frequently in the back, but often passing round to the region of the umbilicus; these are often diagnosed as suffering from some other abdominal lesion. Some patients find the lump and they may even notice that it pulsates. One patient, a civil servant, complained that his heart had moved into his abdomen.

Other symptoms will depend upon the anatomical location of the aneurysm but in



FIG 59 Aortogram showing an abdominal aneurysm arising at a sufficient distance below the renal arteries to make excision and reconstruction the treatment of choice

general terms they consist of pressure effects upon the nearby nerves and veins. When the aneurysm is near a joint the patient may complain of limitation of movement. The clinical features of peripheral aneurysms were well known over 300 years ago, and time has added little to the descriptions of these great men of the past.

It is worth mentioning the findings on auscultation because some still confuse the murmur of an arterio-venous fistula with that of a simple aneurysm An arterial aneurysm is either silent when a stethoscope is placed over it or else a systolic murmur may be heard. If an arterio-venous fistula is present then a full cycle systolic and diastolic machinery murmur will be heard.

Investigations. The first essential is to discover if possible the cause of a patient's

aneurysm. This means a Wassermann reaction, blood sugar estimations if diabetes is suspected, blood cultures in patients likely to have bacterial endocarditis, and biopsy of an accessible nodule in a suspected case of polyarteritis nodosa. In patients with atherosclerosis an estimate of the degree of involvement of the coronary and cerebral vessels is important and here a physician's opinion on the general state of the patient with particular reference to the prognosis of his atherosclerosis, as a whole as opposed to its local manifestation, the aneurysm, is important.

The local investigations of the aneurysm must provide information as to its exact anatomical situation, of the state of the collateral circulation, and of the blood vessels proximal and distal. The modern reconstruction operations in such patients require an accurate pre-operative knowledge of the anatomical position of the aneurysm. This can be assessed on clinical grounds but an arteriogram is of value in many patients. Fig. 59 is an aortogram from a man aged 50 with an aortic aneurysm; it shows an adequate length of aorta between the aneurysm and the patient's renal arteries An aneurysm like this, if it is endangering life, can be replaced by a blood vessel transplant or plastic prosthesis and at operation such a procedure was found to be possible in this patient An arteriogram also shows the position of collateral vessels so that one can plan the incision to avoid as many of them as possible.



FIG 60. Arteriogram showing an occluded popliteal artery This patient had a thrombosed popliteal aneurysm

Complications

RUPTURE

Patients with an aneurysm have a weak spot in their arterial system which is likely to rupture at any time. With aortic aneurysms, either abdominal or thoracic, a period of leakage often precedes frank rupture. The latter event is, of course, fatal within a few moments but a leaking aneurysm of the aorta can be treated surgically. Peripheral arterial aneurysms, apart from those on the cerebral vessels, if they rupture do so into the tissue planes with the production of a large hæmatoma.

Thrombosis

This is a not uncommon complication of a peripheral aneurysm, particularly of the popliteal artery. When the aneurysm thromboses the clot usually spreads into the host artery and these patients develop the symptoms of peripheral ischæmia, either intermittent claudication, rest pain, or gangrene. The following clinical history illustrates a fairly typical case. A shopkeeper aged 52 was quite well; he suddenly developed pain in the calf of the left leg after walking 30 yards and a sensation of extreme cold in his foot. The disability was such that he had to go to bed, where he was kept by his doctor for two weeks. He was now sent to hospital and an arteriogram taken. Fig. 60 shows the state of affairs at this time: the popliteal artery is occluded and the collateral circulation is poor. Up till now the question that the patient might have an aneurysm was not considered but, in view of his poor peripheral blood flow, reconstruction of the popliteal artery with an artery graft was taken. The specimen removed at operation is shown in Fig. 61: it is a thrombosed saccular aneurysm of the popliteal artery with occlusion of the main vessel on each side of the sac. The post-operative arteriogram is shown in Fig. 62. This patient is now at work without claudication 4 years later.

Peripheral Emboli

As stated earlier in this chapter, aneurysms often have a great deal of clot in their walls, portions of this may separate and lodge in vessels peripheral to the aneurysm. This complication is of particular importance in the subclavian aneurysm which is sometimes seen in association with a cervical rib; these patients develop small areas of gangrene in their fingers due in many cases to emboli lodging in the digital arteries.

Enlargement with Pressure on Nearby Structures

Most aneurysms increase slowly in size with the passage of time. Thoracic aneurysms are liable to erode the bodies of the adjacent vertebræ when root pains develop. The function of other nerves may be interfered with, particularly the recurrent laryngeal, the cervical sympathetic chain, and the phrenic nerves Veins too may be occluded when œdema of the limb distal to an aneurysm results

Dissection

This complication may occur at the site of a pre-existing aneurysm but often this acute catastrophe is the first abnormality of which the patient complains A dissecting aneurysm usually arises in an aorta which is atheromatous but the vessel may be surprisingly normal The following is a typical case history of this complication. A middle-aged man was painting the ceiling of a room when he was seized with severe pain in the lower left chest and upper abdomen and at the same time his legs went numb and cold On examination he had no pulses palpable below the umbilicus, an electrocardiogram was normal and he was referred to as a saddle embolus of the abdominal aorta. The patient by the time we saw him had no pulse in either the left common carotid or left subclavian arteries and the lower limbs were still pulseless. He developed a right hemiplegia and died. In this patient a dissecting aneurysm had arisen from a split in the intima at the top of the descending aorta, the extravasation of blood in the aortic wall having first spread



FIG 61 Specimen removed from the patient whose arteriogram is shown in Fig. 60

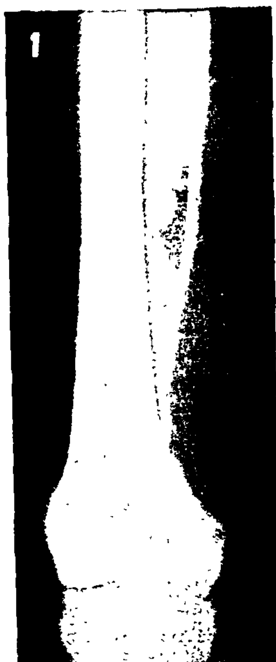


FIG. 62 Post-operative arteriogram from the patient illustrated in Figs. 60 and 61. A homologous arterial transplant has been inserted.

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within it could clot. In more recent times other methods have been tried, notably excision, procedures designed to reinforce the wall of an aneurysm and reconstruction operations.

Arterial Ligature

This ancient operation was described at least 1,500 years ago. One of the first surgeons to write on arterial ligation was Aetius, who in the 6th century described a technique for ligating the brachial artery above an aneurysm. Through the centuries a very extensive literature has grown up on this subject, but it is probable that most of the surgeons who wrote these interesting papers had little practical experience of the operation. The tendency to base opinions upon the results in one patient was as strong in the past as it is today. An exception was John Hunter, who based his operation on a sound footing; he had tied the femoral artery in Hunter's canal on six occasions for popliteal aneurysm before he permitted his assistant, Home, to publish their results, and in one case when the limb was dissected after the patient had died 15 months later the aneurysm was found to have thrombosed.

Surgeons placed the ligatures in a variety of positions relative to the aneurysm. All suffered from two disadvantages; if the method was effective in producing a firm clot in the aneurysm then the risk of gangrene was considerable, and if the limb survived the aneurysm remained because of the efficient collateral circulation.

Another method of considerable antiquity was to incise the sac after a tourniquet had been placed around the limb, to evacuate the clot and then to tie the artery where it entered and left the sac. No attempt was made to excise the sac wall; this was packed and the wound allowed to heal by second intention.

Other Methods Designed to Promote Thrombosis within the Sac

Acupuncture or needling was a method which consisted of passing several long needles into the sac. The idea was that if the points of the needles were correctly placed they would scratch the intimal lining of the sac with each pulsation and clotting would follow.

The Best Method of Making an Aneurysm Thrombose Appears to be Wiring

Linton (1951) has modernized this operation and he recommends its use in aortic aneurysms. He introduces a fine trocar and cannula into the sac through which is threaded stainless steel wire; a large quantity of wire should be inserted usually several hundred feet—he has inserted 700 feet. The idea is that the wire will coil up in the sac; that the blood will clot around it, but that a central channel should remain to maintain the circulation in leaking aneurysms as well as those with intact walls.

A modification is to pass an electric current through a short length of wire within the sac, but this method has produced emboli and rupture

Wrapping in Cellophane

Polythene cellophane produces an intense fibrosis when introduced into the tissues of the human body. This property has been used in the treatment of aortic aneurysms. The sac is exposed and polythene cellophane placed against the adventitia either in the form of a sheet or in small sections. It is important to realize that not all cellophanes produce fibrosis; in fact some are inert in the tissues and cause no reaction. Cellophanes differ

down and occluded the iliac arteries; later it spread up to involve the left common carotid and subclavian vessels.

Prognosis.

The mere presence of an aneurysm is not an indication for active treatment. It must be causing symptoms or threatening the patient's life. The untreated prognosis of an aneurysm depends upon several factors, particularly its cause and location. Colt in 1927 studied a large number of cases, collected from various sources, and he found that the average survival period from diagnoses of 503 patients with thoracic aneurysms and 121 with abdominal aneurysms was less than two years; 82 women with an aortic aneurysm lived on the average three months longer than the men. He also noticed that the survival period of a patient with an aortic aneurysm was twice as great if he was over 60 when the condition was first diagnosed than if he was 35 years of age or younger. These figures paint a very gloomy picture and many consider that the outlook is not so bad. Colt, however, excluded all dissecting aneurysms from his series. Many patients with an aortic aneurysm live for many years without trouble but their number must be relatively few and particularly in patients below 60 years of age, the poor prognosis justifies energetic treatment.

Peripheral aneurysms are not as serious a threat to life if they are in the limbs, but none the less they usually cause considerable inconvenience to the patient. In the case of aneurysms of the cerebral vessels or of the main branches of the aorta life is threatened and the outlook is poor.

Treatment

The first essential is to treat the cause but this is usually a prelude to the treatment of the aneurysm itself. A patient with a mycotic aneurysm should have his bacterial endocarditis controlled before surgery is considered, and polyarteritis nodosa should be treated with cortisone. Both these diseases were, until a few years ago, fatal in nearly every case but now antibiotics frequently cure bacterial endocarditis, and cortisone controls polyarteritis nodosa, but this drug must be taken regularly in maintenance doses. There is, of course, no cure for atherosclerosis, but many of these patients are diabetics and this must be treated. Syphilis, too, should be treated if present.

Medical Treatment

Beyond the essential measure of treating the cause, if it be found, there is no efficient medical treatment for an aneurysm; limitation of activity may prolong life by delaying rupture but the aneurysm remains Certain procedures were used in the past, notably compression which was designed to produce thrombosis of a peripheral aneurysm and the injection of sclerosing fluids into the sac to obtain the same result. Both methods have been abandoned and may be considered to be obsolete, the former because it was rarely successful except in small peripheral arteries, and the latter because of the risk of either rupture or peripheral emboli.

Surgical Treatment

The aims of surgery in this field have been directed along various lines. The earliest efforts were designed to reduce the blood flow through an aneurysm so that the blood

Arterio-venous Fistulæ

(Holman, 1937)

This lesion usually follows an arterial injury and is therefore commoner in wartime, but it may be congenital in origin or follow a closed injury, as in the case of the carotid artery, cavernous sinus, fistula seen after a fractured skull, or a surgical operation (Rob and Eastcott, 1954) or an abscess, if this lies between an artery and a vein, they occasionally form within a tumour, or they may follow the rupture of an atherosclerotic aneurysm.



Fig 63 An arterio-venous fistula between the femoral vessels. Note the false sac and the metallic fragment which produced this lesion

We recently saw an example of this latter event: a man aged 56 was admitted to a hospital more than 300 miles from London suffering from a ruptured aneurysm of the abdominal aorta He survived the journey to St. Mary's hospital and on admission was suffering severe pain because the extravasation of blood had passed into his right thigh and produced intense spasm of the psoas and other muscles. After suitable preparation an emergency operation was performed. A large atherosclerotic aneurysm of the aorta was found with a rupture of its posterior and right wall; the extravasated blood had passed behind the inferior vena cava and into the muscle sheaths of the right iliac fossa and right thigh In addition, a large arterio-venous communication had developed between the aorta and the vena cava where the vena caval wall had given way. In our view, it was

because different plastisers are used in their manufacture; in the case of polythene cellophane the plastiser is dicetylphosphate and it is this substance which produces the intense fibrous tissue reaction. As an alternative to wrapping an aortic aneurysm in polythene cellophane, Berman and Hull (1952) have injected dicetylphosphate mixed with olive oil around the aneurysm. In theory this should produce as much reaction as the operative procedure, but in my experience neither procedure is of real value.

Excision without Reconstruction

This operation replaced arterial ligature in the treatment of peripheral aneurysms during the latter part of the last century. It had two advantages: cure was certain and gangrene was no more likely to occur. It is still the best way of treating an aneurysm arising in an artery which can be sacrificed without risk to the patient. In certain cases the operation may be combined with sympathectomy. In our opinion if sympathectomy is to be performed it is best to do it at the same time as the aneurysm is excised. The reason for this is that the vasodilatation produced by sympathectomy is greatest during the first hours after excision of an aneurysm.

Endo-Aneurysmorrhaphy

This operation, which was introduced by Matas, may be performed in one of three ways, restorative, reconstructive, and obliterative endo-aneurysmorrhaphy. In the restorative operation the sac is opened after the circulation through it has been controlled and sutures are inserted in such a way that the opening into the vessel is tightly sewn up without occluding the original lumen of the artery; the sac is then obliterated by sutures. Reconstructive endo-aneurysmorrhaphy is a similar operation except that a new lumen is formed for the artery from the sac wall and in the case of obliterative endo-aneurysmorrhaphy both the sac and the artery are completely occluded. The disadvantage of both the restorative and reconstructive operations has been the high recurrence rate.

Excision with Reconstruction

This is the most satisfactory way to treat an aneurysm of a main vessel because if successful the blood flow returns to normal. Reconstruction is best performed with either an autogenous vein graft, a homologous arterial transplant or a plastic prosthesis.

In 1907 Lexer stated that there were three possible ways of reconstructing a blood vessel—lateral suture, end-to-end anastomosis and a blood vessel graft. He reported in 1913 that he had resected three arterial aneurysms and restored continuity in each patient with an autogenous vein graft; two were alive and well with patent grafts and one had died after six days, but the graft was found to be patent and intact. In his writings Lexer gives credit to Carrel for his pioneer researches into the suturing of blood vessels. Carrel is in fact the father of modern reconstructive vascular surgery and the technique used today differs but little from his published in 1907. Few remember today that Carrel was awarded the Nobel prize in physiology and medicine in 1912 for his work on the suture of blood vessels and on the transplantation of blood vessels and organs, and that his experimental arterial bank worked well 40 years before the first human arterial bank, using a similar method of storage, was introduced by Gross and his colleagues in Boston (1949).

Treatment. Occasionally a small fistula may close spontaneously but the majority require surgical treatment, either because of the symptoms they cause or because of the probability of cardiac failure. A fistula on a small vessel such as the posterior tibial may be excised or treated by the operation of quadruple ligation. It is important to remember that the adjacent nerve is usually adherent to the sac of an arterio-venous fistula and this must be looked for and preserved in all cases.

The Time for Operation

There is considerable disagreement on the correct time for operation in a patient with a fistula between an important artery and vein. Experience in Korea has led some surgeons to advocate early intervention, a procedure which was also advocated by a minority of surgeons in both the first and second world wars. In our view, early intervention is a mistake except in cases which appear likely to rupture or in whom signs of cardiac insufficiency appear. The reason for this is that an arterio-venous fistula is a first-class stimulus to the formation of a collateral circulation. If the surgeon waits 3 months this will have formed; operation now is safe, even if it is not possible to repair the artery gangrene rarely follows. Thrombosis of the main vessel after an early repair may cause gangrene.

Operation

The ideal to aim at is repair of all important vessels. In general lateral repair is less satisfactory than end-to-end suture, and when the gap is too great the defect can be bridged by an autogenous vein graft or homologous arterial transplant (*see* pages 167–70).

In some patients an arterial repair is impossible and the best alternative is quadruple ligation or, if this is impossible, proximal ligation of both the artery and the vein. It is unnecessary to combine ligation with sympathectomy in these patients because of the first-class collateral circulation, except in those patients operated on within a few days or weeks of the injury.

There is one procedure which should never be performed in these patients and that is ligature of the artery proximal to the fistula only (an exception is the carotid-cavernous sinus fistula) because of the high incidence of gangrene which follows. This is because the blood from the collateral circulation flows back via the intact vein and not into the periphery (*see* Fig. 64).

The post-operative course is usually satisfactory but this is the only operation in which minimal blood loss can do harm. Closing the fistula results in a normal circulation with a greatly increased blood volume; usually hæmorrhage during the operation corrects this and blood transfusion is often needed, but if little blood has been lost and perhaps a transfusion given unnecessarily then heart failure may follow, particularly if the patient presented with signs of cardiac insufficiency before the operation. The correct treatment of this is to bleed the patient and reduce the blood volume to normal.

Congenital Arterio-venous Fistulæ (Robertson, 1956). A typical arterio-venous fistula is a patent ductus arteriosus but congenital arterio-venous communications are by no means uncommon in the peripheral vascular system. In the past they have been known by other names such as cirsoid aneurysm, pulsating angioma, and racemose aneurysm. The fact that arteries and veins develop from a common capillary network and that a

this which saved the patient's life because he bled into his venous system and not his tissues. The segment of aorta was resected and replaced with a plastic prosthesis, the vena cava repaired and the patient made a good recovery.

The Clinical and Pathological Features of an arterio-venous fistula differ in many important respects from those of a simple aneurysm. There are three types of arterio-venous fistula: the aneurysmal varix where the communication is direct without an intervening sac, the varicose aneurysm (Fig. 63) with a false aneurysmal sac, and the congenital malformation which will be described under a separate heading. The artery proximal to an arterio-venous fistula becomes dilated and the wall thinned, distally it is smaller than the normal vessel; the vein particularly on the proximal side of a fistula becomes dilated and hypertrophied.

If the patient has a false sac or a long-standing fistula with very dilated vessels then there will be an aneurysm, but in many patients there is no aneurysm and this is why the term arterio-venous aneurysm is best abandoned. Palpation over an arterio-venous fistula reveals the characteristic thrill and on auscultation the full cycle machinery murmur will be heard, both the thrill and murmur being maximal over the site of the fistula and conducted up and down the parent vessels for a variable distance. Another characteristic clinical feature is the bradycardia phenomenon present in all patients with large communications. Closure of the fistula usually by direct digital pressure immediately slows the pulse rate and raises the systolic and diastolic blood pressures; opening the fistula returns them to their previous level. The degree of slowing of the pulse gives a good idea of the size of the arterio-venous communication; with occlusion of a small fistula it remains unchanged and with a large fistula it may reach 50 or more points. One of our patients had a fistula between the common iliac vessels of 12 years' standing; occlusion of this by pressure on his abdominal aorta slowed his pulse rate from 140 to 80

Distal to an arterio-venous fistula the blood flow is reduced and the skin temperature lowered, although the peripheral pulses are usually palpable. In some long-standing cases the skin temperature and blood flow distal to the fistula may be raised due to the excellent collateral circulation which usually develops. This state of affairs with a raised skin temperature is always present in the region of the fistula and, in patients of growing age, will lead to limb lengthening due to the increased blood supply of an epiphysis near to an arterio-venous fistula. The veins of the limb may be dilated, varicose and pulsatile and the limb may be swollen and œdematous

Systemic Changes and Investigations. A patient with a moderate sized or large arterio-venous fistula has a raised blood volume and an increased cardiac output. In the untreated patient this may lead eventually to auricular fibrillation, cardiac failure, and death. The heart size of such a patient is increased and this will show on an X-ray film. The total red and white blood cell count will be raised as will be the hæmoglobin content. The plasma proteins are often elevated as may be some of the plasma electrolytes; for example, the chlorides and the oxygen content of the venous blood distal to the fistula will be raised.

Arteriography. In many patients this is unnecessary, the size and site of the fistula being assessed with sufficient accuracy on clinical grounds alone, but this investigation is of value whenever the diagnosis is in doubt or the site of the fistula cannot be determined with sufficient accuracy. Due to the rapid blood flow the results of arteriography may be disappointing.

these away from the scalp, working from the deep surface. Finally, amputation may be required when severe hæmorrhage or ulceration occurs in a patient with the diffuse type of fistula.

Vascular Injuries

An artery, a vein, or both, may be involved and the result may be ligature or repair of the vessel, thrombosis, an aneurysm or a traumatic arterio-venous fistula. These injuries are much commoner in war but they are by no means rare in peace-time. Butchers are particularly liable to this injury; one patient of ours, a young butcher, stabbed himself twice in the groin; the femoral artery was divided above and below the profunda branch and the femoral vein was injured as well. Artery forceps applied as a first aid measure made direct suture impossible and so two homologous arterial transplants were inserted, one proximal and one distal to the profunda femoris artery and a venous autograft from the internal saphenous vein used to bridge the gap in the femoral vein.

The following Table I is a combination of the results of arterial ligation in World War I as recorded by Makins and in World War II by De Bakey and Simeone. The high incidence of amputations is due to the fact that these were war wounds and in many patients the missile which damaged the artery damaged the collateral circulation as well; also these patients were often shocked and this interferes with the development of the collateral circulation. In civilian practice the incidence of amputation would be lower but many patients in whom the limb survives are left with an ischæmic limb and suffer from such symptoms as intermittent claudication

TABLE I

AMPUTATIONS AFTER ARTERIAL INJURY IN WAR

(Combined British Army World War 1 (Makins, 1919) and U.S. Army World War 2 (De Bakey and Simeone, 1946)

Artery	Number of Patients	Amputations
Aorta	8	7 (87 5%)
Subclavian	61	10 (16 4%)
Axillary	182	37 (26 4%)
Brachial	801	171 (21 3%)
Radial and Ulnar	28	11 (39 3%)
Common Iliac	14	8 (57 1%)
External Iliac	34	14 (41 0%)
Femoral	883	349 (39 5%)
Popliteal	646	426 (65 9%)
Anterior and Posterior Tibial	98	64 (65·3%)

The initial treatment of such a patient is to control the bleeding by direct pressure, a pressure dressing, arterial ligation or, as a last resort, a tourniquet. The patient is then treated in the way outlined on page 158 (acute arterial occlusion) and sent to hospital as quickly as possible. Here arterial repair should be the surgeon's aim in all cases of division of a major artery using one of the methods discussed on pages 170–72. Figure 65 is an arteriogram from a patient whose common femoral artery and its profunda and superficial femoral branches had been ligated 5 years before during a varicose vein

vessel which is an artery at one stage of development may be a vein at another stage explains their origin. It is surprising that these lesions are not more common. Usually there are multiple communications, a fact which makes treatment extremely difficult.

Clinically there are two types of congenital arterio-venous fistula; the generalized which presents as a big limb usually both longer and larger than its fellow often with localized visible angimatous malformations in which superficial veins can sometimes be seen to pulsate, and the localized where there is a mass of distended pulsating blood

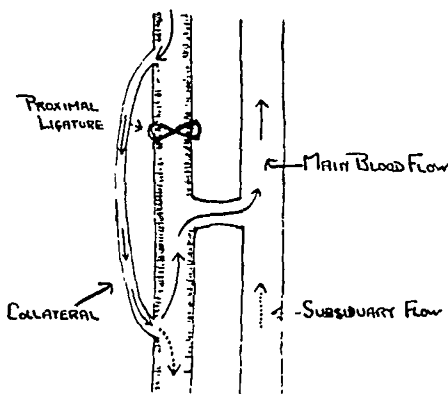


Fig 64 Diagram to show why proximal ligature of the artery without that of the accompanying vein is often disastrous in patients with an arterio-venous fistula.

vessels. A typical example of the latter may be seen in the scalp usually arising from the branches of the superficial temporal vessels. In many patients it is impossible to demonstrate the actual fistulæ either clinical or radiologically, but others have the typical bruit, full cycle murmur, brachycardia phenomenon and arteriographic appearances of an arterio-venous fistula

Treatment. In many patients with a big limb and no systemic changes, treatment is not required but in others energetic measures are required. Again, proximal ligation of the artery alone should not be performed but ligation of the artery and vein may be of help. Exploration to close the fistulæ themselves is nearly always fruitless because, not only are the communications numerous, but they may lie within the substance of a bone. Excision of the whole lesion is the correct treatment for the localized type but this is not often possible and subtotal excision, combined when necessary with a local amputation, is usually the most practical alternative In the case of communications between the superficial temporal vessels this may be accomplished by ligating the external carotid artery, turning down a scalp flap containing the mass of pulsating vessels and dissecting

as atherosclerosis or diabetes and, of course, any local factor such as a tight plaster, an area of anæsthesia or pressure as occurs when a bed sore forms. Terms such as diabetic gangrene are best dropped; a diabetic may develop gangrene because of atherosclerosis, neuropathy or infection; it is important, however, to look for diabetes in every patient who has gangrene.

Gangrene from Arterial Occlusion. Occlusion of a main artery causes gangrene if the collateral circulation is damaged or inadequate. Occlusion of small arteries causes



FIG 66. The foot of a patient aged 61 who had venous gangrene. The arterial tree was normal Ilio-femoral thrombophlebitis was followed by occlusion of the small veins and venules in the gangrenous area She also had a carcinoma of the pancreas.

gangrene particularly when the lesions are multiple or when a terminal vessel such as a digital artery is involved. Before gangrene develops the patient may suffer from REST PAIN and this may be of two types: ischæmic neuritis and erythralgia. Erythralgia is a severe burning pain made worse by warmth or dependency and relieved by elevating or cooling the affected limb. Ischæmic neuritis is either a severe aching or throbbing pain felt in the deeper portions of the toes and foot or an associated superficial pain which is paroxysmal, burning and often agonizing; both of these pains of ischæmic neuritis are worse at night, improved by dependency and aggravated by elevation.

Gangrene from arterial occlusion is usually due to an atherosclerotic thrombosis but

operation; the collateral circulation appeared to be excellent but she developed intermittent claudication after walking a distance of 150 yards, a symptom which was relieved by the insertion of a homologous arterial transplant.

An injury may affect any artery in another way and that is by TRAUMATIC ARTERIAL SPASM with the associated complication of ISCHÆMIC CONTRACTURE, an abnormality which may also follow complete organic interruption of the



FIG 65 The collateral circulation which develops after ligature of the common femoral artery with its profunda and superficial femoral branches. In spite of its apparent efficiency the patient developed the symptom of intermittent claudication after walking a distance of 150 yards

vessel. Traumatic arterial spasm is seen in its classical and most serious form after an injury near the elbow joint, particularly a supracondylar fracture, if untreated Volkmann's ischæmic contracture results. The treatment is to reduce the fracture, extend the elbow and loosen splints or plasters to remove the pressure from the brachial artery and, if improvement does not soon occur, expose the vessel, do a periarterial sympathectomy and bathe the vessel in a solution of 2½ per cent papaverine sulphate (Kinmonth and Hadfield, 1952) If the spasm still persists and is reasonably localized the contracted segment of artery should be removed and replaced by a blood vessel graft or transplant.

Gangrene and Rest Pain. Gangrene may be defined as massive death of tissue and be due to a variety of causes, all of which depend upon reduction of the blood flow, either arterial, venous, or both. Other factors which play a part are infection (whitlows, gas gangrene), the patient's general health (anæmia, heart failure), general diseases such

69 is the foot of an old lady of 76; she had gangrene of the toe and of the centre of her foot. Both the posterior tibial and dorsalis pedis pulses were palpable; the 2nd and 3rd toes with the corresponding metatarsals and soft parts were removed and the wound healed by first intention. A very useful amputation is the transmetatarsal but it often





Figs 67 and 68 This patient aged 28 had lost one leg from thromboangiitis obliterans. The arteriograms are from his remaining leg, Fig 67 before and Fig. 68 after operation The foot was gangrenous but a vein graft from the distal femoral artery to the posterior tibial vessel has restored the blood flow.

fails in patients who do not have either a posterior tibial or dorsalis pedis pulse. As with all amputations in patients with arterial insufficiency, the surgeon's technique must be meticulous; the skin edges must never be touched with forceps, hæmostasis must be absolute and the wound closed without tension in two layers, one of the deep fascia and one of the skin. The place of sympathectomy as an aid to the healing of an amputation stump requires discussion. In my view this is of value when the healing is in doubt and the operation should be performed at the same time as the amputation. The reason for this is that the cutaneous vasodilatation and hyperæmia are maximal in the first days after a ganglionectomy

other causes include: thromboangiitis obliterans, an embolus, injuries, Raynaud's phenomenon, the cryopathies, infections (gas gangrene, carbuncles).

Diabetic gangrene is a term no longer in general use. A patient who has diabetes may develop infective gangrene (a carbuncle or whitlow), he may have a neuropathic ulcer or he may develop atherosclerosis and suffer from atherosclerotic gangrene.

Gangrene from Venous Occlusion (Martin, 1954, Moore and Scott, 1956). This rare event occurs when occlusion of a main vein such as the iliofemoral is associated with occlusion of the venules in the part which becomes gangrenous. An alternative explanation is that severe arteriolar spasm following the main venous occlusion is the cause of the gangrene. It is most likely to occur in those with a carcinoma or some intercurrent disease such as ulcerative colitis. Figure 66 is the leg and foot of such a patient. A cross section of the thigh after amputation showed a normal femoral artery with complete occlusion of the accompanying veins. The condition is recognized by the fact that the whole limb is swollen and œdematous, the gangrenous areas are blue and the adjacent tissues warm Reduction of the œdema by elevation may enable the surgeon to feel the arterial pulses and, in case of doubt, an arteriogram will show a normal arterial tree.

Management of Gangrene and Threatened Gangrene

(Rob, 1957, Mavor, 1957)

The rare venous form of gangrene is best treated by elevation and anticoagulants. Other forms of gangrene present a major problem and every effort should be made to preserve the limb but when this is not possible amputation should not be unduly delayed.

The care of the acutely ischæmic limb has already been discussed on pages 156–60, and many of the measures described there are of help when the arterial occlusion has been of more gradual onset. The first essential is to decide what is the cause of the patient's gangrene or threatened gangrene and to treat this cause; diabetes, for example, should be controlled and a patient with thromboangiitis obliterans should stop smoking. In some patients medical measures of the type already described will limit the process and healing occur, and great care must be taken to protect such a limb in the future with careful chiropody and protection from all forms of injury.

Of the surgical measures sympathetic ganglionectomy takes pride of place as the most useful. This measure is of particular value in those patients with some element of spasm as a cause of their gangrene but it also helps by improving the collateral circulation around a thrombosis and by producing cutaneous vasodilatation.

Another measure which will have an increasingly important place in certain patients is an arterial reconstruction operation. About 25 per cent of patients with gangrene of the toes or feet have a lesion of their arteries which is anatomically suitable for a reconstruction operation and when the alternative is a major amputation there can be few, if any, contraindications. Figures 55 (*a*) and (*b*) and 67 and 68 illustrate two successful cases. The first patient had an aortic occlusion as the cause of her gangrene and the second a popliteal thrombosis, whilst Figures 67 and 68 show that this procedure can be successful in thromboangiitis obliterans, although the thromboses in this disease are usually too peripheral for this type of operation to be possible.

Amputations. There has been a steady trend towards conservative amputations in patients with gangrene, the infective gangrene of diabetes being the best example. Figure

necrosis of the skin due to pressure on bony points such as the sacrum, heels or iliac crests during long surgical operations and prolonged bed rest. In addition, pressure may cause ulceration when a plaster splint has been applied unevenly and too tightly.

The best treatment is prevention with proper precautions by the medical and nursing staff. Once established, these lesions heal very slowly, skin grafting may be required.

Arterial Hypertension

(Pickering, 1955)

This may be primary or secondary to some disease or abnormality. With increasing knowledge more and more patients are found to have a cause for their hypertension, when no cause is found the patient is said to be suffering from essential hypertension.

It is first necessary to treat the cause if one is present, and in many cases this treatment is surgical and includes such procedures as: the correction of a coarctation of the aorta, nephrectomy for a unilateral renal lesion, adrenalectomy for Cushing's syndrome or phæochromocytoma, thyroidectomy for hyperthyroidism, the relief of raised intracranial pressure, etc. Of recent years atheroma of one renal artery has been found to cause hypertension; this lesion is sometimes treatable by operation.

When the hypertension is primary or essential, the treatment is in the first place medical. In the past many of these patients were treated surgically but with the introduction of the modern hypotensive drugs operation has become rarely necessary. The main disadvantage of surgery was the difficulty of deciding which patients would react well. Some idea of the fall in the number of patients treated surgically may be given by the following figures from my own practice. Between 1946 and 1951 I operated on 117 patients for essential hypertension, between 1951 and 1957 on 9.

The Operation. This may take one or both of two forms: sympathectomy or adrenalectomy. In general the former is the most satisfactory. The earlier sympathectomies for hypertension were those of Crile, Adson, and Peet; today the Smithwick procedure is the most popular. This consists of removal of the sympathetic chain from the 7th dorsal to the 3rd lumbar ganglion, together with the splanchnic nerves. Each side is operated on separately via a thoracolumbar incision with an interval of about two weeks between the two procedures.

The modern position of surgery in this disease has been well summarized by Pickering. He states that· "Subtotal or total adrenalectomy has now little or no place in the treatment of essential hypertension" and that. "Sympathectomy has a very strikingly beneficial effect on a few patients, a good effect on some and, perhaps, no effect on others. It is a major operation, with a low mortality in experienced hands but with some postoperative sequelæ such as severe pain of a causalgic type, and giddiness and palpitations on standing and on effort. The major difficulty, which has not yet been solved, is to determine in advance which patients will react well and which badly."

The Cryopathies

(Learmonth and Ungley, 1943, Ungley, Channel, and Richards, 1945)

These may be defined as diseases due to cold and from the point of view of the peripheral vascular system include: frost-bite, trench foot, immersion foot, and chilblains. Frost-bite, trench foot, and immersion foot are all commoner in wartime but in civilian

The next best amputation after a transmetatarsal is the Syme's amputation. This procedure gained a bad reputation in Britain because of the unsatisfactory results which followed Syme's amputations performed for trench foot during the first world war. The lesson from this is that trench foot is a vascular abnormality and Syme's amputation is only occasionally of value in patients with peripheral vascular disease. A below-knee amputation is very useful in peripheral vascular disease, particularly in those patients who have a palpable popliteal pulse or are suffering from thromboangiitis obliterans, but it is a mistake to use this procedure too frequently and it rarely succeeds in patients with gangrene due to an extensive atherosclerotic thrombosis of the superficial femoral artery. The Stokes Gritti amputation through the femoral condyles with attachment of the patella to the end of the femur is a useful procedure in elderly patients and, lastly, the above-knee amputation, although rightly considered today a final admission of failure, becomes necessary eventually in many patients with gangrene due to senile obliterative arterial disease.



FIG 69 The foot of a diabetic patient aged 76 The 2nd and 3rd toes with the corresponding metatarsals have been removed for gangrene with sound primary healing

Gangrene due to arterial disease rarely necessitates an amputation in the upper limb but here amputations of the fingers are often unduly delayed. Patients with Raynaud's phenomenon often develop a gangrenous finger tip often due to thrombosis of the digital arteries. The gangrene in these patients may heal after sympathectomy but often it persists accompanied by rest pain and a useless digit. An amputation through the distal portion of the proximal phalanx heals well and improves the function of the hand.

Trophic Ulcers and Pressure Sores

Patients with anæsthesia of the skin as a result of a neurological abnormality are particularly liable to develop deep penetrating ulcers, particularly on the soles of the feet; vascular insufficiency increases this tendency Pressure sores may occur from ischæmic

Raynaud's Phenomenon

This phenomenon consists of intermittent attacks of pallor of the extremities usually the fingers but the toes, ears, nose, and even the tongue may be affected. Cyanosis may be associated with the pallor and the part feels numb and cold. As the attack passes off the part may become hot and red and the patient may complain of a burning pain.

The first essential when confronted with a patient suffering from Raynaud's phenomenon is to search for the cause; in a male this is frequently thromboangiitis obliterans. Other causes include atherosclerosis, often with thrombosis of a digital artery, a high titre of cold agglutanins in the serum, polyarteritis nodosa and allied diseases, the use of vibrating tools and the thoracic outlet syndrome.

Primary Raynaud's Phenomenon or Raynaud's Disease. This may be defined as Raynaud's phenomenon occurring in a patient with no evidence of organic arterial obstruction or associated disease. It is much commoner in women between 20 and 30 years of age and there is often a history of similar abnormalities in the family. In its early stages the patient suffers from intermittent attacks due to spasm of the digital arteries. Later permanent nutritional changes occur and finally sclerodactyly and gangrene. The attacks are brought on by exposure to cold, particularly cold water, and at first occur only in the winter but later throughout the year. Later superficial ulcers develop, particularly at the finger tips; these may be very painful and the fingers and thumb become tapered from the tips with stiffness and even subluxation of the joints; and finally gangrene develops particularly if the part has been exposed to excessive heat during an attack.

In spite of much research, the exact cause of Raynaud's phenomenon remains unknown. We do know that the attacks are due to spasm of the digital arteries and that later these arteries may thrombose but, in spite of much work by Raynaud (1888) and others including Sir Thomas Lewis (1929) and Goetz (1949), the mechanism of and reason for the attacks remains in doubt.

Treatment. The hands should be protected from cold and the patient should stop smoking. Drugs such as Ronicol or Priscol may help if given in big doses. Surgical treatment consists of sympathectomy, which is a most effective measure when the feet are affected but is often of only temporary value when the hands are involved. In general, however, sympathectomy, even for patients with involvement of the hands, is a worthwhile procedure but should be performed if possible before gangrene has occurred. Once gangrene is established it is probably better to amputate the fingers than allow the patient to suffer months or years of pain, and it is often surprising how well a distal type of digital amputation heals in these patients. Of the many drugs which have been used in the treatment of this disease dibenyline has the advantage that it is effective both before or after sympathetic denervation, and therefore may be prescribed if symptoms recur after operation, the usual dose is 10 mgm. 3 times a day.

Secondary Raynaud's Phenomenon is seen much more frequently than the primary phenomenon. Lewis and Pickering (1934) considered that gangrene followed secondary Raynaud's phenomenon only, or at any rate only occurs when a digital artery has thrombosed. The management of a patient with secondary Raynaud's phenomenon depends first and foremost upon the correct diagnosis and treatment of the primary cause, and then the actual Raynaud's phenomenon may be helped in the way already outlined. Many of the primary causes such as the various forms of obliterative arterial disease have

practice frost-bite is often associated with pre-existing arterial disease. Frost-bite closely resembles a burn and, like it, may be classified according to the depth of tissue destruction Today this means those with partial thickness and those with full thickness skin loss. Trench foot and immersion foot are now considered to be similar lesions due to long exposure to wet and cold, not necessarily of a sufficient degree to freeze the tissues. An added factor is muscle inertia as occurs in a small open boat or a slit trench.

The first symptoms of trench or immersion foot are coldness and numbness. The feet swell after removal of the boots and may become discoloured from subcutaneous or intracutaneous hæmorrhages. Later the foot becomes hyperæmic and very painful; this may last for a month or longer. At any time gangrene may occur. Some recover, others recover after tissue loss and a further group develop a hypersensitive extremity with hyperhidrosis and contractures of the toes or fingers.

Treatment. The cryopathies are more easily prevented than cured. Education of Service personnel does much to limit their incidence in wartime. Frost-bite is best treated by slow thawing with reflex vasodilatation to increase the blood flow in the frozen part. It is also of value to prescribe heparin to limit intravascular thrombosis. The local treatment of necrotic areas is similar to that prescribed for a burn but the patient should be warned that a part once frost-bitten will have an increased sensitivity to cold. Trench and immersion foot are treated in the same way with the difference that local cooling with a fan or even ice bags may be needed to control the pain during the hyperæmic stage.

Chilblains. These are commoner in the British Isles than in the U.S.A. or Canada. Efficient home heating has been cited as a reason for the lower incidence in the latter two countries. Acute chilblains usually occur in patients below 20 years of age. There is slight œdema, a bluish-red colour and itching or burning; the extremities—fingers, toes, and ears are usually affected If the patient scratches the skin becomes broken and infection results. The best treatment is the provision of a warm and dry environment plus the treatment of infection with antibiotics if necessary.

Chronic chilblains have also been called erythrocyanosis and Bazin's disease or erythema induratum. A similar lesion is seen on the limbs of some patients after anterior poliomyelitis. The cause appears to be repeated vascular spasm due to cold. The best treatment is again the provision of a warm and dry environment; when this is not possible sympathetic ganglionectomy may help

Erythrocyanosis Frigida

This disease is seen almost exclusively in women, is much commoner in the north-west of England than in the south. It is associated with hypoplasia of the arteries and veins, is chronic and is frequently present in patients with severe chronic chilblains. The leg and ankle are swollen with bluish discoloured patches on the skin and the whole limb is cold. Summer or movement to a warmer climate brings relief (Rose, 1956).

Poliomyelitis

Some patients after an attack of paretic poliomyelitis are left with a cold blue limb, the skin of which may ulcerate. In cold damp weather such a limb is likely to develop severe chilblains. These patients, particularly if the lower limb is at fault, receive considerable benefit from sympathectomy with the limb becoming pink and warm and the ulcers healing.

In most patients the clinical features are so mild that no treatment is necessary but if the condition is severe very good results follow sympathectomy when the feet or hands become pink, warm, and dry.

Erythromelalgia

This rare condition is characterized by attacks of burning pain in one or more extremities associated with redness of the skin, the attack starting when the environmental temperature has reached a critical level. The disease is usually bilateral and usually affects the feet; the pain may be very severe indeed. In our view Telford and Simmons (1940) are correct when they state that good results follow sympathectomy but, because others have reported worsening of this condition after sympathectomy, we always perform a novocaine sympathetic nerve block first; if this is effective the operation is performed. Of three patients all have been relieved.

Tiblalis Anticus Syndrome

This subject was reviewed in 1953 by Moritz, who found the reports of 27 cases and added four of his own. The syndrome consists of necrosis of the anterior tibial group of muscles with paralysis of the anterior tibial nerve. There may be no obvious cause for the condition arising spontaneously after exercise in an otherwise healthy young male or the patient may have developed an acute arterial occlusion such as that due to an embolus (Watson, 1955) or they may suffer from an arterial disease or a recent injury. The anterior tibial group of muscles become tender, swollen, painful, there is usually increased sensitivity or paræsthesia in the cutaneous area supplied by the anterior tibial nerve and the patient may have a mild pyrexia. A foot drop can occur but this may be prevented by contracture and fibrosis of the anterior tibial muscles. Treatment is essentially conservative with bed rest and splintage, although paravertebral blocks may be of value. If the swelling and pain appear to be excessive decompression of the anterior tibial compartment by a fasciotomy should be considered but this is only of value early before the muscles have become completely necrotic.

Polyarteritis Nodosa and Allied Diseases

(Lovell and Rose, 1955)

This disease and similar associated lesions such as giant-celled arteritis causes necrosis and inflammation of the wall of small and medium sized arteries which may result in arterial occlusion or occasionally aneurysm formation. The onset is usually fairly rapid and the early general symptoms include fever, tachycardia, loss of weight, generalized aches and pains and tenderness in the limbs. The E.S.R. is raised, many patients are anæmic and there is usually an eosinophilia. The local manifestations include renal involvement which may lead to anuria or the development of hypertension; the alimentary tract may be the source of pain, diarrhœa, vomiting, or hæmorrhage; skin involvement produces multiple subcutaneous nodules usually near the ankles; involvement of the peripheral nervous system produces scattered asymmetrical polyneuritis and involvement of the coronary arteries congestive cardiac failure.

Surgically this disease is of importance because of the problem which it sets in diagnosis and because the surgeon is frequently asked to confirm the diagnosis with a muscle biopsy. The treatment is with cortisone in large doses, initially 200 mg. per day by

already been discussed. Another, the thoracic outlet syndrome, will be discussed now, and other causes include scleroderma, rheumatoid arthritis, leprosy, and ergot poisoning

Thoracic Outlet Syndrome

The vascular and nervous supply of the upper limb may be disturbed as a result of a variety of abnormalities which may occur at the thoracic outlet; amongst these may be included: a cervical rib (Eden, 1939), the scalenus anticus syndrome (Naffziger and Grant, 1938), the costoclavicular syndrome (Telford and Mottershead, 1947) and of importance in the differential diagnosis because it may produce similar symptoms as regards the nervous system is prolapse of a cervical intervertebral disc.

The patient may give a history of pain, paræsthesia and numbness, worse in the early hours of the morning and felt mainly in the areas supplied by the ulnar nerve. The vascular symptoms may simulate Raynaud's phenomenon or the patient may develop a fusiform aneurysm of the subclavian artery from which emboli may reach the fingers or hand and cause gangrene.

The treatment depends upon the cause but considerable relief may be obtained by physiotherapy to the muscles of the shoulder girdle. In patients with an obvious cervical rib removal relieves most of the symptoms and is a worthwhile procedure. In our experience scalenotomy has not been a particularly effective procedure and we now always advise that it be combined with resection of part of the first rib.

Carpal Tunnel Syndrome

This lesion is by no means uncommon and, although the symptoms are mainly nervous, a number of these patients reach a surgeon who is interested in diseases of the peripheral vascular system. The patient complains of pain and paræsthesia in the distribution of the median nerve in the hand. Often both hands are involved and examination shows wasting of those muscles of the hand which are supplied by the median nerve; later in a severe case there is anæsthesia over the skin of this region. The main differential diagnosis is from a lesion of a cervical intervertebral disc.

The treatment is to divide the transverse carpal ligament completely. Under general anæsthesia the limb is exsanguinated and a short transverse incision made in one of the skin creases of the wrist just proximal to this ligament. The median nerve is identified and a blunt dissector passed between the ligament and the nerve. The ligament is now divided with scissors and the wound closed. This is an effective and simple procedure but it is a curious fact that division of one ligament may relieve the symptoms in the less severely affected hand as well

Acrocyanosis

Patients with this abnormality suffer from painless cyanosis of the hands and feet which is worse in the cold weather The disease is commoner in women, it rarely if ever progresses to gangrene and is often confused with Raynaud's phenomenon, although the two diseases are very dissimilar. The ætiology and pathological physiology are less well understood than they are in Raynaud's phenomenon but Lewis and Landis (1930) have shown that the cyanosis is not due to obstruction of the main venous drainage. In their opinion the abnormality is an increased tone of the arterioles with a secondary dilatation of the capillaries and venules

limb; for example, a patient who has lost his left upper limb and years later develops angina pectoris feels the pain in his phantom limb. The usual explanation is that once the cerebral cortex has fully registered the whole body image, this registration persists in spite of the loss of part of the body.

Treatment of a painful phantom limb is first to prevent its occurrence by performing an efficient amputation with high clean division of the main nerve trunks, and then to explain to the patient that the presence of a phantom limb is normal, that some fleeting painful sensations are usual and that these will largely disappear after he starts to use his prosthesis. If, in spite of this, pain develops a search should be made for a local cause such as infection of the bone end and then, if this is negative, percussion of the nerve trunk as advocated by Ritchie Russell (1949) is a most useful measure; but in our view the best treatment for this condition is the fitting and use of an artificial limb.

Tumours of Vascular Origin

Angiomas. These tumours are usually of congenital origin and are usually classified as capillary and cavernous and as hæmangiomas and lymphangiomas, making four possible types of tumours. In addition, many tumours are mixed in type and some contain a large proportion of some other mesodermal tissues such as is seen in a hæmangio-lipoma or -fibroma.

Capillary Hæmangiomas

Capillary hæmangiomas are by far the commonest vascular tumour in clinical practice. They are known as the spider nævus, the cutaneous nævus, telangiectasia when multiple and the port wine stain when large. Whilst they usually occur in or just deep to the skin, they may occur on mucous membranes and here both capillary and cavernous hæmangiomas may cause repeated bleeding particularly from the alimentary tract and produce a diagnostic problem of great difficulty.

Cavernous hæmangiomas are usually seen in the subcutaneous tissues but can develop in any organ of the body. They consist of dilated thin-walled blood vessels, grow slowly during life and never metastasize. Clinically they present as soft, ill-defined swellings which may be reduced in size by pressure or sometimes by elevation of the part. Often they have a blue colour where the vessels come close to the skin or where there is an associated capillary hæmangioma.

Lymphangiomas

Lymphangiomas are similar in nature, the capillary type being the most common. A classical example of the cavernous type is a CYSTIC HYGROMA. Occasionally cavernous lymphangiomas develop in the limbs when they must be distinguished from the much more common lymphœdema due to lymphatic obstruction.

Malignant Angiomas

Malignant angiomas are uncommon and are referred to by various writers as hæmangio-sarcomas and hæmangio-endotheliomas. Both tumours vary greatly in the degree of their malignancy, some hæmangio-endotheliomas being almost benign whilst some vascular sarcomas are very malignant, and here the distinction between a hæmangio-sarcoma and a vascular form of spindle-celled sarcoma may be difficult to make. A

mouth in four doses and this is later reduced to a level which keeps the symptoms suppressed.

Temporal Arteritis. The temporal artery is tender and clinically inflamed. The patient complains of headache. The disease is uncommon below the age of 55 years and most of the patients develop the symptoms of an atherosclerotic thrombosis of another artery during the next year or so. Excision of the tender artery may relieve the headache and establishes the diagnosis.

Panniculitis. There are general symptoms similar to those of polyarteritis and the diagnosis is made because subcutaneous nodules at first raised, red, tender, later depressed and painless develop particularly on the lower limbs and buttocks. Microscopical examination shows that the nodules are areas of fat necrosis probably due to thrombosis of small arterioles.

Other diseases such as disseminated lupus erythematosus, erythema nodosum, dermatomyositis, etc., which may be included in this group will be mentioned only for completeness; the reader is referred to medical textbooks for further details

Causalgia and the Painful Phantom Limb

Causalgia follows partial division or only bruising of a nerve, usually the median, and from a clinical point of view it is a good plan to speak of major and minor causalgia. Minor causalgia follows injury often to a digital nerve or an amputation and consists of a moderate or severe burning pain with increased sweating and warmth of the part concerned. Major causalgia, on the other hand, is a very rare occurrence today, although it was seen more frequently after the war of 1914–18, and once seen it is never forgotten because it is one of man's worst afflictions. The pain is burning in type and of extreme severity, whilst the involved part, usually the hand, is red, hot, shiny, sweating, and hyperæsthetic. The pain is spasmodic and between spasms the sufferer sits as far away as possible from his fellow men, protecting his hand by all means within his power from any movement or other stimulus which might initiate an attack of pain. The cause of this pain has never been discovered but it may well be that the pain arises in some abnormality of the nerve endings in the skin.

Treatment. Minor causalgia, if it fails to respond to reassurance, time, physiotherapy and other local measures, usually responds to sympathetic ganglionectomy, particularly if a sympathetic nerve block has already relieved the pain. In the case of digital nerve lesions neurolysis or resection of the contused segment and resuture may be effective. On the other hand, major causalgia does not in our experience respond to sympathectomy although it may be relieved by resection of the damaged segment of nerve followed by resuture. It is said that division of the nerve distal to the point of damage may relieve major causalgia. We have no experience of this but, although in the case of the median nerve it would be followed by considerable loss of function, it would be preferable to suicide which may follow in patients with this terrible but very uncommon disability.

Phantom Limb. After every amputation except those performed during early infancy the patient has the sensation of a phantom limb. In the vast majority this causes no inconvenience apart from an occasional attack of pain but a minority complain bitterly of pain in the phantom limb or even of persistence of the pain for which the amputation was performed It is of interest that the later development of a pain in another part of the body which would be referred to the limb if it were in position is felt in the phantom

even be considered as suffering from anorexia nervosa. Fortunately the treatment is easy; under local or general anæsthesia the tumour can be excised and the symptoms cured. Very occasionally the tumours are multiple and then each one should be excised.

Carotid Body Tumours (Lecompte, 1951). These uncommon lesions are usually found at the carotid bifurcation but may occur in other sites such as the glomus jugular near to the base of the skull. Microscopical examination shows that they are composed of masses of epithelioid cells resembling those of the normal carotid body, there are few mitodic figures and most of the tumours are benign.

The patient complains of a tumour which has been present for many years and which has enlarged slowly during this time. Examination shows the tumour to be adjacent to the bifurcation of the carotid artery and either to present transmitted or expansile pulsation. The explanation of this is that some tumours are solid and these transmit pulsation from the carotid arteries to which the tumour is often densely adherent, whilst others are extremely vascular (Fig. 70) and sponge-like. The vascular type of carotid body tumour pulsates like an aneurysm, has a systolic or sometimes a full cycle murmur over it and may be mistaken for either of these lesions. When in doubt an arteriogram will establish the diagnosis.

Treatment. These tumours do not respond to radiotherapy and in our view it is a mistake to attempt treatment other than by surgical excision because of the additional difficulties that radiotherapy makes for the surgeon. In the past many have advised that these tumours should receive no treatment at all because of the failure of radiotherapy to influence the course of the tumour and because of the very high mortality which followed surgical excision, but recent advances have changed this. In our view these patients should be operated on under hypothermia (29°C–30°C), the carotid vessels proximal and distal clamped and an attempt then made to dissect the tumour away from the carotid arteries. This is often possible in the solid type of tumour but rarely, if ever, possible in the case of the vascular tumours, in which case the involved segment of vessel should be resected and continuity of the internal carotid artery restored with an arterial graft or transplant. The advantage of hypothermia is that it makes it possible to occlude the carotid arteries for a long period without risk of cerebral damage and this, combined with the greater use of arterial reconstruction operations, has made the operation safe when performed by an experienced surgeon. It must be stressed that the vascular type of carotid body tumour presents technical problems which are unlikely to be surmounted outside a special centre for vascular surgery.

Arterial Reconstruction Operations

(Rob, Eastcott, and Owen, 1956)

The flow through an artery may be restored by one of the following surgical procedures: an embolectomy, direct suture, thrombo-endarterectomy, the insertion of an autogenous vein graft, an autogenous, homologous or heterologous arterial transplant, a plastic implant or in the case of an aneurysm by the operation of endoaneurysmorrhaphy.

Embolectomy. Embolic obstruction of the aortic bifurcation is best treated surgically and the same holds for many emboli which lodge in the femoral, popliteal, and other arteries. The vessel should be exposed just proximal to the embolus and controlled with

particular variety of hæmangio-sarcoma is the so-called Kaposi (1872) tumour. These are multiple angiosarcomas usually of the skin of the lower limb; the subcutaneous tumours are blue in colour and if untreated visceral deposits may develop. In many patients, however, a good response occurs to radiotherapy when the lesions are still confined to the subcutaneous tissues.

Treatment. Many small capillary hæmangiomas are noticed in infancy and here it is



Fig 70 Arteriogram showing the extremely vascular nature of some carotid body tumours The tumour in this patient had enlarged in spite of 5,000 R by radiotherapy Excision with reconstruction of the internal carotid artery was successful

better to leave the lesion for some months or years because many remain stationary in size as the child grows and thereby become more and more inconspicuous. For larger lesions a variety of measures have been used; the most effective are radiotherapy and surgical excision but good results have also been recorded following electrocoagulation and the injection of sclerosants, particularly in the treatment of lesions unsuitable for either of the first two methods.

Glomus Tumours. These small tumours arise in the glomus of the skin and are most commonly found in the limbs, particularly the fingers. They are painful swellings usually about ⅛th of an inch in diameter situated in most patients near a finger-tip or under a nail. The pain may be extreme and touching the finger or changing its temperature may provoke a severe spasm of pain In some patients the pain may be so severe and so easily provoked that the patient finds a normal activity such as eating a great trial and they may

and each common iliac artery, to open the aorta above the clot after it had been controlled with a clamp, to remove the clot by suction until a good back flow occurs from each iliac artery and then to clamp the common iliac arteries and close the aortic incision. As before, it is important to avoid clamping the distal vessels, in this case the common iliac arteries, until all the clot has been removed. In addition, hæmorrhage from the middle sacral and lower lumbar arteries may be troublesome. If this is so then they should be temporarily occluded with small bulldog clamps. Another important point is that there is sometimes an associated embolus of the inferior mesenteric artery and the presence of normal pulsation in this vessel should be checked before the abdomen is closed. If an embolus of this artery is found it should be removed. The main disadvantage of the transperitoneal approach is that the patient frequently develops post-operative paralytic ileus, but if this complication is anticipated by gastric aspiration and intravenous feeding little harm results.

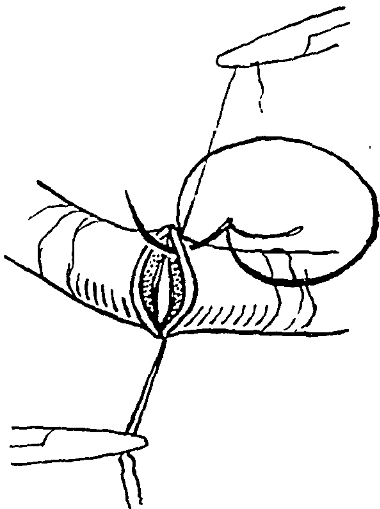


Fig. 72 Technique of vascular suture—insertion of the two everting mattress sutures.

In the past surgeons were loth to perform an embolectomy if a time of more than 6 or 8 hours had elapsed. Today this no longer holds: if the peripheral circulation is unsatisfactory but massive gangrene is not established then the vessel can be explored days or even weeks later and, should an embolectomy be impossible, some other form of arterial reconstruction operation used. In some patients there may be doubt about the exact site of the embolus; in this case an arteriogram is of great value because it enables the surgeon to plan his operation properly.

Direct Suture. This is the best method of arterial reconstruction and it is surprising how frequently it is possible to perform it, particularly in elderly people where the vessel may be lengthened and tortuous, thus permitting the bridging of a considerable defect by direct suture (Fig 71). In general, it is better to perform an end-to-end anastomosis than a lateral suture, and after an injury the results of end-to-end suture are much better.

The modern technique of vascular anastomosis using 2 or 3 stay sutures and then a continuous everting mattress or over and over suture of fine silk was worked out by

a tape or clamp, then opened with a longitudinal incision about 1 in. in length and the embolus removed with great care and gentleness, using a polythene tube attached to a sucker. Once a good back flow has been established a clamp may be applied distal to the incision in the artery, after which 5,000 units of heparin should be injected into the vessel below the distal clamp, the adventitia removed from the arterial wall near to the incision and this should then be closed with a continuous over and over suture of fine silk. It is

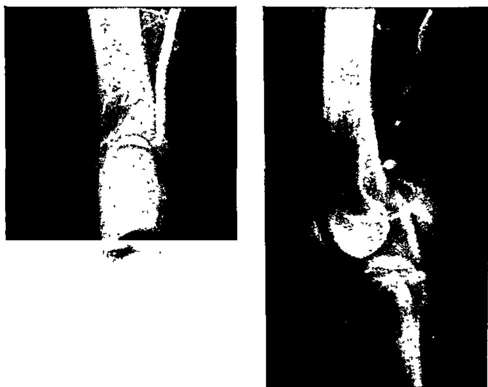


FIG 71. A popliteal aneurysm which was resected and continuity restored by a direct end-to-end anastomosis The aneurysm was due to atherosclerosis and the patient was aged 61

most important when performing an embolectomy to avoid clamping the vessel distal to the embolus before all the clot has been removed. Failure to do this may result in the fragmentation of the embolus where the clamp has been applied with the result that the blood flow is never re-established or more peripheral emboli follow removal of the clamps. It is important to remember that all emboli should be examined microscopically; in one of my patients with a popliteal embolus an unsuspected carcinoma of the bronchus was diagnosed because the embolus was composed of oat type carcinoma cells

Aortic Embolectomy. The saddle embolus of the bifurcation of the abdominal aorta has been approached in a variety of ways, but two main techniques have been evolved. In one the surgeon exposes both common femoral arteries and, if they are patent, opens both vessels and attempts to remove the embolus with suction on two polythene tubes passed up through the openings in the femoral arteries towards the aortic bifurcation. Once a satisfactory flow has been re-established clamps are applied and the incisions in the femoral arteries closed. In my view the best technique is to expose the aortic bifurcation via a transperitoneal abdominal incision, to isolate the aorta above the bifurcation

and each common iliac artery, to open the aorta above the clot after it had been controlled with a clamp, to remove the clot by suction until a good back flow occurs from each iliac artery and then to clamp the common iliac arteries and close the aortic incision. As before, it is important to avoid clamping the distal vessels, in this case the common iliac arteries, until all the clot has been removed. In addition, hæmorrhage from the middle sacral and lower lumbar arteries may be troublesome. If this is so then they should be temporarily occluded with small bulldog clamps. Another important point is that there is sometimes an associated embolus of the inferior mesenteric artery and the presence of normal pulsation in this vessel should be checked before the abdomen is closed. If an embolus of this artery is found it should be removed. The main disadvantage of the transperitoneal approach is that the patient frequently develops post-operative paralytic ileus, but if this complication is anticipated by gastric aspiration and intravenous feeding little harm results.

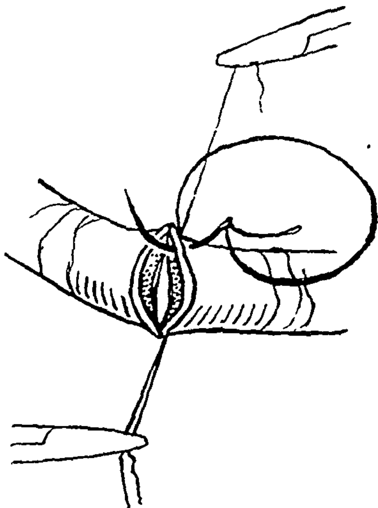


Fig 72 Technique of vascular suture—insertion of the two everting mattress sutures.

In the past surgeons were loth to perform an embolectomy if a time of more than 6 or 8 hours had elapsed Today this no longer holds· if the peripheral circulation is unsatisfactory but massive gangrene is not established then the vessel can be explored days or even weeks later and, should an embolectomy be impossible, some other form of arterial reconstruction operation used. In some patients there may be doubt about the exact site of the embolus; in this case an arteriogram is of great value because it enables the surgeon to plan his operation properly.

Direct Suture. This is the best method of arterial reconstruction and it is surprising how frequently it is possible to perform it, particularly in elderly people where the vessel may be lengthened and tortuous, thus permitting the bridging of a considerable defect by direct suture (Fig. 71). In general, it is better to perform an end-to-end anastomosis than a lateral suture, and after an injury the results of end-to-end suture are much better.

The modern technique of vascular anastomosis using 2 or 3 stay sutures and then a continuous everting mattress or over and over suture of fine silk was worked out by

Carrel (1907) and has not altered since. The first step is to strip back the adventitia for a distance of about one centimetre from the vessel on each side of the proposed suture line. This step is important because if it is omitted the adventitia gets caught in the suture with the result that the approximation becomes imperfect and pieces of adventitia get drawn with the suture into the lumen of the vessel, which greatly increases the incidence of thrombosis. After removal of the adventitia the ends of the vessel are trimmed and made smooth and two everting mattress sutures placed at opposite ends of one diameter of the

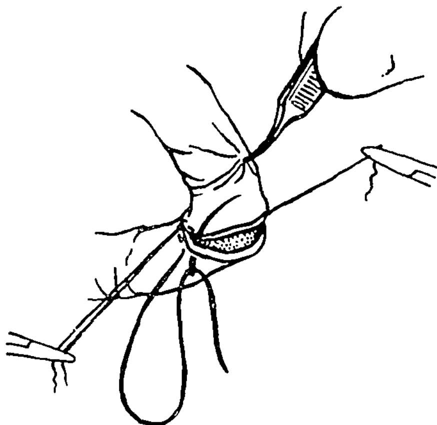


FIG 73 Technique of vascular suture—rotation of the vessel to give adequate exposure *for insertion of the posterior half of the suture line*

proposed circular suture line (Fig. 72). The anterior portion of the anastomosis is now performed using a continuous over and over suture. In my view this is better than an everting mattress stitch because it constricts the lumen less. The posterior half of the anastomosis is now inserted rotating the vessel first to the left and then to the right in order to get good exposure. This rotation is achieved by passing the free ends of the interrupted sutures in turn behind the vessel and applying gentle traction (Fig. 73). After the anastomosis has been completed the distal clamp is removed first and the occluded segment allowed to fill from below. The proximal clamp is now removed and firm, steady pressure applied with a swab for 5 minutes This is a most important step; unless the hæmorrhage from the suture line is so severe that it cannot be controlled by firm pressure, the surgeon should resist the temptation to insert extra sutures. The most alarming hæmorrhage from a suture line usually stops if the surgeon waits patiently and applies steady pressure for 5 full minutes; the reason is that the pressure of the arterial flow

tightens the continuous suture and blood clots in any small gaps which are left. If bleeding persists after this period of pressure one or more interrupted sutures may be inserted as necessary.

Suture Materials and Instruments. Fine silk sutures moistened with sterile paraffin oil and mounted on small curved round-bodied atraumatic needles are best for vascular

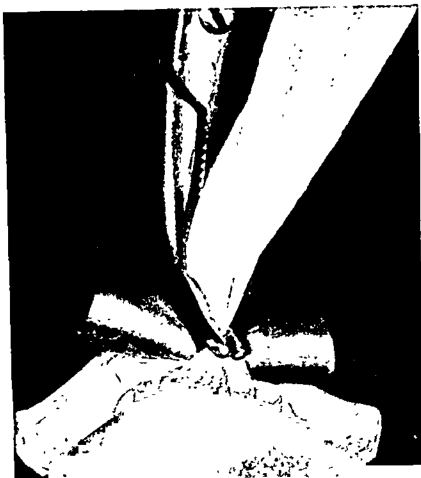


Fig 74 The tape tourniquet method of arterial control. The short length of rubber tubing should have a diameter about equal to that of the artery.

suture; we use 0000 silk for the aorta and 00000 silk for other vessels. Other special instruments which are of assistance include fine-toothed and smooth dissecting forceps, fine scissors and a small light needle holder. As regards vascular clamps, a variety are available and many are unnecessary or actually harmful for use in peripheral vascular surgery (Rob and Henson, 1956) When possible the tape tourniquet is the best method for the occlusion of an artery; when this cannot be used a bulldog clamp is satisfactory for all vessels except the aorta, and here a Pott's coarctation clamp gives good control without damaging the vessel excessively The tape tourniquet is applied (Fig. 74) by passing a wide tape round the vessel, placing a short length of rubber tubing of a diameter about equal to that of the artery on the front of the segment which is to be occluded and then pulling the tape tight so that the vessel is occluded by the pressure of the tape against the rubber tube. The tape is then held in position with a cholecystectomy or other suitable clamp. The advantages of this method of arterial control are that no

special instruments are required, that the method is less traumatic than many of the special arterial clamps and it is efficient. The main disadvantage is that a fair length of the vessel has to be mobilized to apply the tape and perform the anastomosis comfortably.

Thrombo-endarterectomy. This operation was developed by dos Santos (1947) and in our view, if the patients are selected with great care, it is the best method of restoring the blood flow through a thrombosed artery. Table II (Rob, 1956) gives our results with the various arterial reconstruction procedures and it will be seen that the results with this method have been the best.

TABLE 2

290 ARTERIAL RECONSTRUCTION OPERATIONS

	Number of Patients	Dead (Including Operation Deaths)	Thrombosed Early and Late	Patent Today
Direct suture	27	3	2	22
Thrombo-endarterectomy	50	4	9	37
Autogenous vein	31	4	15	12
Homologous artery	124	12	38	74
Plastic cloth	32	8	0	24
P.V A sponge	26	6	12	8

The operation of thrombo-endarterectomy is best reserved for patients with a localized occlusion of a large vessel such as the aorta or common iliac arteries. Some idea of the strictness of the selection which we have applied may be appreciated when it is stated that of 73 patients with occlusion of the aorta or common iliac arteries (Leriche's syndrome) only 42 or 54 per cent were considered suitable for a direct surgical operation and only 16 of these 42 for thrombo-endarterectomy but 15 of these patients have patent vessels today.

TECHNIQUE OF PERFORMING THROMBO-ENDARTERECTOMY

The occluded vessel should be exposed and mobilized for a short distance above and below the thrombosed segment. Between these points the vessel should be freed throughout the anterior two-thirds of its circumference. Clamps are then applied above and below the thrombus. 5,000 units of heparin may be injected into the artery below the distal clamp and a longitudinal incision made throughout the length of the thrombosed artery. This incision passes through the adventitia and outer part of the media where a well-defined plane of cleavage is encountered. The thrombus, the intima, and the inner portion of the media can now be separated from the remaining media and adventitia with a blunt dissector and removed. At each end the intima should be cut clearly so as to avoid loose tags and it is a good plan to carry the thrombo-endarterectomy proximally and distally for a distance of about 1 cm. beyond the completely occluded segment. The vessel is now washed with saline to remove loose debris and closed with a continuous over and over suture. Some surgeons use a special ring stripper which is passed up through a small incision in the artery below and the thrombus removed through a second small incision proximal to the occlusion. This method is of special value for long occlusions of the femoral and popliteal arteries but in my view a bypass arterial transplant is a more effective method of dealing with this abnormality.

Autogenous Vein Grafting. This procedure was used before the first world war by Lexer (1913) and Pringle (1913) and during that conflict by Weglowski (1925) and many others. Between that time and the end of the second world war it was rarely practised but recently this technique has been used again The use of a vein graft to replace a segment of artery has certain limitations, the most important of which is that the vein ruptures in many cases if the artery to be replaced lies within a body cavity. The advantages of this technique include the ready availability of autogenous veins and the fact that they are autogenous and therefore survive transplantation, but as Table II shows our results with this technique have been disappointing.

After the artery has been prepared a length of vein is made ready, the most suitable being the long saphenous. It is isolated and its branches are tied. It is then reversed so that the distal end of the vein is anastomosed to the proximal end of the artery. When the recipient artery lies close to the donor vein, a good method is that devised by Weglowski (1925). The distal end of the vein is anastomosed to the proximal artery (Fig. 75) and the clamps removed so that the patient has a temporary arterio-venous fistula. The clamps are then reapplied, the vein and artery near to the anastomosis washed free of blood and the second anastomosis performed. The advantages of this technique are that it is impossible for the surgeon to fail to reverse the vein and the second anastomosis is performed more easily because the vein will have been stretched first.

It is important when inserting a vein graft to bridge a defect in an artery that the graft should be put in under considerable tension Failure to do this results in the vein graft assuming a corkscrew-like appearance when blood under arterial pressure is admitted to it; eddies are then set up and thrombosis may be the result.

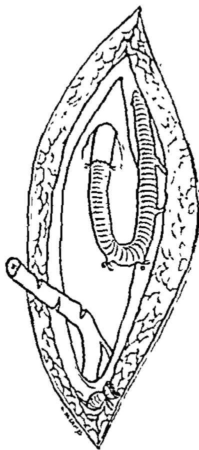


Fig. 75. Weglowski's method for inserting a vein graft. The distal end of the saphenous vein has been anastomosed to the artery proximal to the lesion. This is allowed to run for a few minutes as an arterio-venous fistula before the distal anastomosis is made.

Arterial Transplants. An arterial transplant may be autogenous, homologous, or heterologous. Autogenous arterial grafts are rarely used because of the obvious lack of suitable donor material, and heterologous transplants give unsatisfactory results. This means that in clinical practice the homologous transplant is the only form of arterial transplant in general use. To use homologous arterial transplants it is essential to have an arterial bank and we find freeze-drying to be the most convenient method (Eastcott, Holt, Peacock, and Rob, 1954).

Arterial Banking

The donor should be less than 35 years of age if the vessels are to be freeze-dried and he should not have suffered from a transmittable disease. If the body has been kept in a refrigerated chamber an interval of 24 hours may be permitted before the arteries are

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(*a*)



(*b*)

FIG 77 (*a*), (*b*) A long bypass arterial homograft inserted between the common iliac and popliteal arteries. The reason for operating was gangrene of the toes Note the end-to-side anastomosis particularly behind the patellar

removed from the body. At room temperature in temperate climates it is wise to remove the arteries within 8 hours of death. The arteries are best removed with a full aseptic technique as for a surgical operation and each branch should be left about 1 cm. long. The whole aorta, iliac, femoral, popliteal and carotid vessels should be removed from each donor and placed in a bowl of sterile isotonic saline. As an additional precaution the vessels may be sterilized by irradiation (Meeker and Gross, 1951) either ethylene oxide

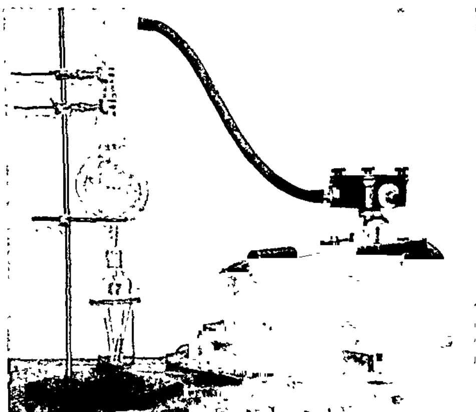


FIG. 76 The simple freeze-drying apparatus which we have used at St Mary's Hospital since the early part of 1953 Before that we had stored our arteries in the frozen state since 1950 and still use this method when we do not have to transport our arteries from St Mary's Hospital

(Hufnagel, Rabil, and Reid, 1953), beta-proprio-lactone (Szilagyi, Overhulse, and Lo Grippo, 1954) or antibiotics (Fisher, Adams, Wilde, and Fisher, 1956). The vessels are now cut to the required length, placed in sterile tubes, frozen to −79°C by immersion in a mixture of alcohol and solid carbon dioxide (dry ice) and then subjected to drying by a high vacuum pump. Figure 76 is a diagram illustrating the simple freeze-drying apparatus which we use and which we made ourselves at a cost of approximately £70. The advantage of freeze-drying over other methods of arterial banking is that the vessels can be kept for indefinite periods at room temperatures and transported with ease.

TECHNIQUE OF ARTERIAL GRAFTING

The graft is prepared by rehydration in the case of the freeze-dried product or rapid thawing if it is frozen. The branches are then tied with fine silk and the ends prepared by stripping the adventitia as already described. The graft may then be inserted by one of



(*a*)



(*b*)

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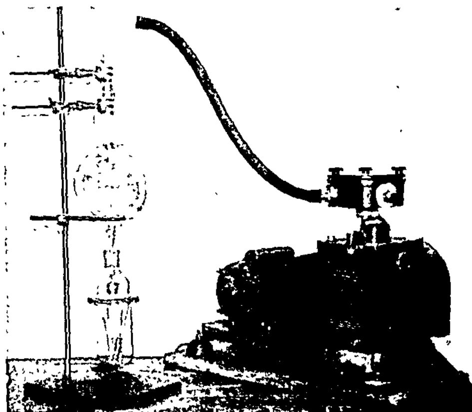


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muscle as well. The dissection should now be continued until the scalenus anticus muscle has been exposed; this is made easier by retraction medially of the internal jugular vein and division of one or two minor branches of the subclavian artery as they pass across the line of the incision. The scalenus anticus muscle may be identified by the presence of the phrenic nerve which passes obliquely over its anterior surface; this nerve should be retracted medially and the scalenus muscle is then divided. Division of the scalenus muscle exposes the suprapleural membrane (Sibson's fascia) and the dome of the pleura and the whole pleural dome is now freed by careful blunt dissection, preferably with the finger. This should be continued on the medial side as far as the transverse process of the 4th or 5th dorsal vertebra. If the pleura is opened it does not matter, provided that the anæsthetist is informed, but it makes the operation much more difficult.

The surgeon is now confronted with a triangular opening bounded by the jugular vein and carotid artery medially, the subclavian vessels inferiorly and the brachial plexes on the superior and lateral side. Long thin bladed retractors are now inserted and the pleura depressed by pressure of a retractor on a swab. The stellate ganglion may be identified by palpation and its lower portion dissected free. The dissection is now carried down along the sympathetic chain to below the 3rd dorsal ganglion. This dissection must be performed with the greatest care; if hæmorrhage occurs it is best controlled by firm pressure with a small swab on a holder and the bleeding point then either coagulated with diathermy, or if larger, controlled with a Cushing-Mackenzie clip. The ramii communicantes are now divided and the chain removed. It is important to preserve the ramii communicantes from the first thoracic nerve to the stellate ganglion.

Removal of this amount of the stellate ganglion does not cause a Horner's syndrome. This operation, although technically difficult, is from the patient's point of view a minor procedure. It can be performed on both sides at once and even so the patient is able to leave hospital by the fifth post-operative day.

The Lower Limb. Figs. 78, 79, and 80 illustrate an important aspect of this operation. If one assumes that the cutaneous sympathetic supply corresponds even approximately to the arterial supply, then in order to open up the collateral circulation around an arterial occlusion one must denervate the part of the limb in which the occlusion lies. This means that the standard lumbar ganglionectomy with removal of the 2nd and 3rd ganglia should be employed for occlusions of the popliteal artery and distally, that the first lumbar ganglion should be removed when the occlusion lies in the femoral artery, and that the 10th dorsal to the 3rd lumbar ganglia should be removed when the aorta or iliac arteries are thrombosed. The standard lumbar ganglionectomy will now be described when it is desired to remove more of the chain. The 12th rib should be resected, the diaphragm divided and the pleura stripped upwards to expose the lower dorsal ganglia.

A transverse incision is made in the abdominal wall at the level of the umbilicus. It should be about 5 in. long and about two-thirds should be lateral to the linea semilunaris. The peritoneum should not be opened but stripped from the lateral and posterior abdominal walls and retracted medially. On the right this will expose the inferior vena cava and on the left the aorta. The chain is identified by palpation and then isolated by dissection, the second and third lumbar ganglia are removed and, if possible, the first lumbar ganglia, but this is not always possible and when it is considered essential that it should be removed it is wiser to employ an incision which passes through the bed of the 12th rib.

two techniques; the end-to-end or the end-to-side bypass method. In general, the end-to-end anastomosis is best after the excision of an aneurysm or for the repair of an injury, whilst the bypass technique is the method of choice when the reason for operating is an arterial thrombosis. The technique of end-to-end anastomosis is similar to that for direct suture and will not be described again, apart from stressing that the graft must be placed under considerable tension.

The Bypass Technique

The usual common femoral to popliteal bypass graft will be described but similar principles are applied in other regions. The patient is placed on his side in the position described by Rob and Owen (1956) and the operation is best performed by two surgeons working as a synchronous combined team. An incision is made over the common femoral artery and another over the popliteal artery and the two are connected by a tunnel in the approximate line of the subsartorious canal. The arterial transplant is then threaded through the canal and anastomosed without tension to the common femoral and popliteal arteries. The actual end-to-side anastomosis is performed in the following way. The end of the graft is cut obliquely so that a large anastomosis can be made and an appropriate portion of the wall of the host artery is removed. The anastomosis is now performed using two needles with their threads tied together and one needle is used for each half, the two halves of the suture line being inserted at the same time. Fig. 77 (*a*) and (*b*) shows a long bypass homograft inserted for gangrene from the common iliac to popliteal arteries.

Plastic Implant. Many types of plastic material are in use for the replacement of the aorta and its major branches but as yet no satisfactory plastic prosthesis has been found for the replacement of vessels of the size of the human femoral artery and smaller. The aorta and its major branches may be replaced by one of the plastic cloths such as vinyon N, terylene, orlon, or nylon, or by polyvinyl alcohol sponge. It is not possible as yet to say which of these materials is the best but satisfactory early results have been obtained with them all, vinyon N cloth for the longest and polyvinyl alcohol sponge for the shortest time. In our opinion terylene is probably the most satisfactory.

Sympathectomy

This is a valuable procedure, probably the most valuable, in many patients with peripheral vascular diseases. The indications have already been discussed, technique only will be described here. The completeness of a sympathectomy can be assessed by studying the area of skin which has been deprived of sweating.

The Upper Limb. An adequate sympathetic denervation of this part of the body may be obtained by removal of the upper three thoracic ganglia together with the intervening sympathetic chain. If one is operating for hyperhidrosis it is wise to remove one or two more ganglia, otherwise excessive sweating may persist in the lower portion of the axilla.

There are three methods of approaching this portion of the sympathetic chain; the cervical, axillary, and the posterior. In our view this is also the order of their preference and the cervical route will be briefly described. A transverse incision is made just above the clavicle in the line of the skin folds of the neck. The incision should be about 4 or 5 in long and at the inner end it should stop about ½ in from the mid-line. The lateral or clavicular portion of the sternomastoid muscle should be divided and the omohyoid

The complications of an upper thoracic sympathectomy include: Horner's syndrome, abnormal gustatory sweating, excessive dryness of the nose, hæmothorax and pneumothorax, and severe brachial neuritis from the upper thoracic operation; from the lumbar procedure disturbance of sexual function, particularly if both first lumbar ganglia are removed, paralytic ileus and pain particularly in the distribution of the first lumbar nerve.



FIG. 80

FIGS 78, 79, 80 These three illustrations show the area of skin over which autonomic denervation is achieved by removal of the 2nd and 3rd lumbar ganglia (Fig 78), the 1st, 2nd, and 3rd (Fig. 79), and the 10th dorsal to 3rd lumbar ganglia (Fig. 80), and by each is an arteriogram showing that if the area of skin denervation corresponds to the arterial denervation then such an operation is required to open up the collaterals around an arterial occlusion at each of these three levels.

Achilles Tenotomy

This minor procedure (Boyd, Jepson, and James, 1949) is of value in the occasional patient who has very severe intermittent claudication of the calf muscles at 50 to 100 yards and who has good nutrition of the foot. Under local anæsthesia a tenotomy knife is introduced from the lateral side behind the tendo achillis about 2 in. above the attachment of the tendon into the os calcis and the tendon divided. The patient can then walk home and is able to proceed at a slow pace without pain, but there is a tendency for the tendon to reunite and for the pain to recur, but this minor procedure can be repeated as necessary.



Fig 78



Fig 79

arterial catheter introduced by the percutaneous technique from one of these vessels to almost any part of the arterial system. Space does not allow the description of all forms of arteriography, so only one, LUMBAR AORTOGRAPHY (Dos Santos, 1929), will be described. The patient may either be given a general anæsthetic or heavily sedated with pethedine, a method which we prefer. He is then placed face downwards on the X-ray table with a tunnel for film changing beneath his lower trunk, pelvis, and lower limbs. The needle (16 gauge) is then inserted after infiltration with 2½ per cent novocaine 5 in. to the left of the midline at the level of the first lumbar vertebra. It is advanced upwards and medially until it strikes the body of the 12th dorsal vertebra, it is then withdrawn a little and passed to the point of the vertebral body when it enters the aorta. The needle is then attached to a transparent plastic tube and then to a syringe containing saline which is injected very slowly. When all is ready a small test injection is made and a film exposed to confirm the position of the needle, then 20 to 30 ml. of 70 per cent diodone or pyelosil is injected as rapidly as possible and serial films exposed, which may if necessary cover the vascular tree from the site of aortic puncture to the toes.

Arteriography is now a relatively safe procedure but complications do occur and the following have been reported: thrombosis at the site of the injection, hæmorrhage from the needle puncture, damage to nearby structures by a periarterial injection, paraplegia, mesenteric thrombosis and anuria from an aortic injection, sudden deaths from a thoracic aortogram particularly of the arch of the aorta, thrombosis of another artery if already diseased, and sensitivity reactions to the contrast medium.

Phlebography (Gryspeerdt and Crockett, 1953). This may be either orthograde or retrograde and of these two techniques we prefer the orthograde. Under local anæsthesia an injection of 30 ml. of 35 per cent pyelosil is made into a vein on the dorsum of the hand or foot; previously a light tourniquet has been applied to the ankle or wrist to obstruct the superficial veins and ensure that the contrast medium is directed into the deep venous system. The injection should take about 10 seconds and just before its completion a plate under the lower leg is exposed; exactly 10 seconds later the patient performs the Valsalva manœuvre and the thigh plate is exposed. The Valsalva manœuvre forces the contrast medium back into the leg veins and demonstrates the valves.

Lymphangiography (Kinmonth, 1954). This method has been developed by Kinmonth and his colleagues and is likely to be used increasingly in the investigation of these difficult cases. First 10 ml. of 11 per cent patent blue is injected into the skin of the dorsum of the foot and then a short incision is made by a nearby vein, the patent blue will have made the lymphatic visible and it is surprising how easy it is to insert a needle or canula in the lymphatic trunk. 15 to 20 ml. of 35 or 50 per cent pyelosil is then injected into the lymphatic vessels and good visualization of the vessels of the whole limb may be obtained.

DISEASES OF VEINS

Varicose Veins of the Lower Limb. This is one of the commonest abnormalities met with in surgical practice and at least half of the patients who attend hospital on account of an abnormality of the peripheral vascular system do so because of varicose veins.

Anatomy and Physiology

The venous drainage of the superficial tissues of the lower limbs is via the long or internal and short or external saphenous veins, with a small area on the upper part of the

Anticoagulants

In peripheral vascular surgery these may be used during an operation or in the immediate post-operative period, as a short-term measure in the management of a patient with an acute thrombosis or embolus (arterial or venous), or as a long-term measure to prevent further thrombosis in a patient who has obliterative arterial disease.

As already mentioned, we use local heparin during most of our direct surgical operations and if the total dosage does not exceed 5,000 units little trouble will be caused, but if it is necessary to give a larger dose trouble may be experienced when the clamps are removed. In this case protamine sulphate given intravenously works as an efficient and rapid antidote to heparin. Heparin during the immediate post-operative period can be dangerous; the reason is that, even with the most meticulous control, hæmorrhage can occur not only from the arterial suture line but as a general ooze from the wound as a whole. Today we rarely use heparin at this time but when it is necessary consider that it is wise to drain the wound or leave it partially open.

As a short-term measure in an acute arterial embolus or thrombosis or in a venous thrombosis, particularly when there is a risk of a pulmonary embolus, anticoagulant therapy is of special value. We usually start with an initial dose of heparin of about 10,000 units and repeat this once or twice by intravenous injection through a Gordh needle. At the same time as the heparin is begun we give 200 mgm. of Dindevan and then about 100 mgm. twice a day. The heparin is therefore responsible for the first 18–24 hours and after this the Dindevan takes over. Careful control with regular estimations of the prothrombin time is essential. In most cases about ten days' treatment will see the patient through the acute stage and then the question is whether to use long-term therapy or not.

Long-term anticoagulant therapy, although a measure of as yet unproven worth, is in my view worthwhile in patients with obliterative arterial disease because there is a steadily accumulating volume of evidence that it may prevent further thromboses (Lund, 1953, Suzman, 1956). Today we place as many of these patients as possible on Dindevan and, as stated, try to keep them taking this drug for the rest of their lives.

Local anticoagulant therapy via a fine polythene tube placed just proximally to the vascular suture line has been recommended by a number of authors, but tests we have carried out have failed to demonstrate any difference between the clotting time of the blood near to the anastomosis and in the general circulation; we have therefore abandoned the method.

Angiography

It is possible to visualize the arterial, venous or lymphatic systems by angiography and, although the resulting information is largely anatomical, it is of great help in diagnosis and in planning treatment.

Arteriography. Every portion of the arterial tree may be visualized by this technique. We inject 35, 50, or 70 per cent pyelosil or diodone after testing the patient for sensitivity and use a percutaneous technique with sedation but no general anæsthetic in nearly every case. A simple tunnel film changer is to be preferred to costly mechanical changers for arteriography of the limbs because with a good team one can get better visualization of the vessels of the whole limb by this means. The usual sites for arterial injection are the aorta, the common femoral, common carotid, and subclavian arteries, or one may pass an

rupture of a varicose vein after an injury or from a vein in the base of an ulcer. This is most easily stopped by elevation of the limb and direct pressure over the bleeding point. In addition many overweight, middle-aged women with varicose veins suffer also from flat feet, osteoarthritis of the knees and hallux valgus and it is sometimes difficult to decide which abnormality contributes most to their discomfort, but efficient treatment of the veins usually pays.

When examining a patient with varicose veins the surgeon should attempt to obtain information which will enable him to answer the following questions. Which veins are varicose? Which communications between the superficial and deep venous system have incompetent valves? What is the state of the deep venous system and is there a cause for the varices? The first question may be answered by simple inspection and palpation of the limbs when particular attention should be paid to the sapheno-femoral junction and the point where the external saphenous vein enters the popliteal fossa. The location of the incompetent communications can to a large measure be achieved by simple inspection and palpation, where the presence of a cough impulse in the main trunk of the internal saphenous vein in the thigh or in the external saphenous vein in the calf indicates failure of the valves which protect the origins of these veins. In addition, large "blow outs" along the course of the main venous trunks serve to locate some of the incompetent communicating veins, but in most patients it is wise to perform one or more of the various tourniquet tests, not only to assist the location of the incompetent communications but also to answer the next question—what is the state of the deep venous system?

The tourniquet tests (Trendelenburg, 1891, Perthes, 1895, Mahorner and Ochsner, 1936) are performed by laying the patient on a couch and raising the leg to empty the veins. A tourniquet is then placed around the upper portion of the thigh sufficiently tight to obstruct the superficial veins. The patient now stands; if no veins fill within 30 seconds there are no incompetent communications distal to the tourniquet; if veins fill then further tests are required to locate these incompetent communications. The tourniquet is now removed; if there is no immediate filling from above the valves at the sapheno-femoral junction they are competent; immediate filling from above indicates valvular incompetence at this point. The so-called double positive result occurs when there is filling both before and then more after removal of the tourniquet; it indicates incompetence at the sapheno-femoral junction and also below at the junction of the external saphenous with the popliteal vein or via communicating veins. The exact site of incompetent communications below the sapheno-femoral junction can now be determined by applying the tourniquet at various levels, first just above the knee, then below the knee, and repeating the test. The double or treble tourniquet tests are also of value; in the manner already described two or three tourniquets are applied, one at the groin and the other just below the knee and the third, if used, just above the knee. These control both the sapheno-femoral junction and the junction of the external saphenous vein with the popliteal vein, and the third tourniquet controls the large communication between the femoral and saphenous vein which occur here, so that any filling of the superficial varices must be through other incompetent perforating veins. The two or three tourniquets are then released in order from below upwards.

The tourniquet tests serve to demonstrate complete obstruction or valvular incompetence of the deep veins if the patient is asked to walk or mark time with the tourniquet

back of the thigh draining via a number of minor channels into the gluteal veins. The superficial veins of the foot unite to form the internal saphenous vein which passes just in front of the internal malleolus of the ankle joint and the external saphenous vein which passes behind the external malleolus. The internal saphenous vein passes up the inner side of the leg behind the femoral condyle and then up the medial side of the thigh to end by passing through the fossa ovalis to join the common femoral vein. From the surgical point of view certain points in the anatomy of the internal saphenous vein are of great importance; first, the main venous drainage of the skin in the region of the internal malleolus where ulcers are so frequently seen is not to the internal saphenous vein but passes via three or four perforating veins to the deep veins of the calf; second, this is the longest vein in the body and the most frequent site of varicose veins; third, as Dodd and Crockett (1956) have so clearly stated, the venous drainage of the superficial tissues in the erect exercising leg is inwards to the deep veins via the various perforating veins. With exercise the blood in the superficial veins is sucked inwards to the deep veins where the muscles squeeze it towards the heart. The high pressure in the deep veins is not transmitted to the superficial veins during exercise because at every point where the two systems meet there is a valve and the primary cause of varicose veins is the destruction of one or more of these valves so that the superficial veins are made to dilate, become lengthened and tortuous.

The external saphenous vein passes from behind the internal malleolus upwards and across the back of the leg; about halfway up the calf it comes to lie deep to the deep fascia of the leg; it then passes up to the popliteal fossa where it joins the popliteal vein. This is the usual course but there are a number of alterations of which the most frequent is for the vein to pass round the inner side of the thigh to join the internal saphenous vein a few inches below the fossa ovalis.

Ætiology

In addition to the anatomical factors already discussed there are a number of other predisposing factors, of which the most important is hereditary. Pregnancy is also very important but here the exact reason is obscure because the varicose veins usually develop before the uterus is large enough to interfere with the venous return by pressure. Occupation may play a part and it is reasonably well-established that varicose veins are commoner amongst athletes. Varicose veins may be secondary to some other abnormality such as a deep venous thrombosis, a pelvic tumour or an arterio-venous fistula.

The Clinical Picture

The real reason why most patients complain of varicose veins is the disfigurement. In the case of many men this disfigurement is of little importance and they never consult a doctor; on the other hand, most women request active measures to improve the appearance of their legs. In addition many patients complain of an aching pain in the legs worse on standing. This is particularly so in patients with varices of the external saphenous vein and in women because they notice that their varices get larger and ache more when they are menstruating. Some patients suffer from recurrent attacks of phlebitis. Later with the onset of deep venous incompetence, swelling, eczema, pigmentation, and ulceration occur, but these symptoms are really the result of the deep venous lesion and will be discussed under that heading. An uncommon complication is hæmorrhage, either from

although for older patients and those with a previous history of deep venous thrombosis it is better to be content with the more minor procedure of saphenous ligation.

The operation should vary a little from patient to patient but in general terms those with internal or external saphenous incompetence require high ligation and stripping of the appropriate vein or veins, and those with additional incompetent communicating veins, particularly in the postero-medial part of the leg, need individual ligation of each of these.

Internal Saphenous Ligation and Stripping

Under general anæsthesia an incision parallel to the skin crease of the groin is made with its centre over the sapheno-femoral junction 1½ in. below and lateral to the pubic tubercle. A self-retaining retractor is inserted and elevated by an assistant so that the subcutaneous tissues are lifted away from the vein. The internal saphenous vein is now identified and followed to its point of junction with the common femoral vein, all the tributaries of the saphenous vein are divided—this is an important step and the number of tributaries varies from 3 to as many as a dozen. The main internal saphenous vein is now tied close to the sapheno-femoral junction and, to make the procedure safe, a second transfixion ligature is placed just distal to the first.

The surgeon now exposes the internal saphenous vein at the ankle through a small transverse incision. The vein is tied distally, a ligature placed around it and left untied, and the vein opened with sharp scissors. The tip of the stripper (Myers type) is then introduced into the lumen of the vein and passed upwards; frequently it reaches the groin incision, if it does not a small incision is made over its point of arrest and the procedure repeated from there. The tip of the stripper is drawn out of the vein at the proximal end until the shoulder of the stripper reaches the vein in the ankle incision. The vein is then tied to the stripper wire by the shoulder, the vein divided proximal to the distal ligature and just below the transfixion ligature in the groin. A steady strong pull with occasional rotation is now applied to the stripper wire and the whole vein drawn into the groin wound. If the stripper becomes arrested the point of arrest should be exposed surgically and the instrument freed. As soon as the stripper has been withdrawn the whole limb is elevated and firm pressure applied to the bed of the saphenous vein. The ankle wound is now sutured whilst the limb is held elevated by an assistant and a firm bandage applied from the ankle upwards. When the groin is reached the leg is placed on the table and this wound closed in the usual way.

External Saphenous Ligation and Stripping

This is most easily performed with the patient lying face downwards. But when, as is sometimes necessary, it has to be combined with internal saphenous stripping, the limb can be suspended by a sling placed between two lithotomy poles. The surgeon then sits down and exposes the external saphenous vein by looking upwards. An alternative is to operate on such patients under local and nerve block anæsthesia so that they can co-operate by turning over during the procedure.

A transverse incision is made across the popliteal fossa just above the level of the head of the fibula and deepened so that it passes through the deep fascia. Before this the external saphenous vein can be seen through this fascial layer. The vein is dissected free and followed into the popliteal fossa. It is then ligated in the same manner as the internal

in position at each of the points already described. The superficial veins of a patient with normal deep veins empty when he exercises the limb even with a tourniquet in position because the blood is sucked into the deep venous system. However, when the deep veins are thrombosed or the valves are incompetent, exercise under these conditions makes the superficial veins more prominent, the limb becomes cyanosed and the patient is forced to stop walking because of pain. If after a full clinical examination there is still doubt about *the state of the deep veins a phlebogram will settle this point.*

The last question is—what is the cause of the varices? This is best answered by a full clinical examination with particular reference to the lower abdomen and pelvis to exclude pregnancy or a tumour. It is also important to take a careful history with particular reference to deep venous thrombosis of the popliteal or iliofemoral veins or even of the inferior vena cava. An arterio-venous fistula, either congenital or acquired, is another possible cause.

Treatment. Uncomplicated varicose veins may be treated by simple supportive measures, injections and saphenous ligation with or without stripping. Simple supportive measures with an elastic stocking or bandage should only be advised where for some reason such as very poor general health operation is not justified.

INJECTIONS

Injections with a sclerosant such as sodium morrhuate or ethamoline have been widely practised but with the passage of years the true value of the method has been assessed. Today most surgeons reserve it for the treatment of relatively small groups of veins when there is no evidence of valvular incompetence, and its use as an additional measure during the operation of saphenous ligation has been completely abandoned because of the risk of the sclerosant collecting on the valves of the deep veins whilst the patient lies on the operating table and damaging them. On the other hand, injections may be used to tidy up small residual varices which may have persisted after an operation. The reason why injections have been abandoned for all but the most minor varices is the very high recurrence rate.

Using a meticulous aseptic technique and with the patient sitting or lying down, the needle is introduced into one of the varices and 2 ml. of ethamolin injected after which the patient remains at rest for 5 minutes and then is allowed home with a dressing firmly strapped to the injection site. With this technique the complications of injections are few; ethamolin does not cause injection ulcers; with this volume of sclerosant and this technique damage to the deep veins is a rarity; the worst complication is septic thrombophlebitis and this, if it occurs, is due to a fault in the aseptic technique. But even in patients with small isolated groups of varices recurrence is common either by recanalization or by the dilatation of adjacent veins.

OPERATION

Saphenous ligation properly performed with division of all the tributaries at the sapheno-femoral junction, division of the external saphenous vein in the popliteal fossa and division of the main saphenous trunk wherever it was joined by an incompetent communicating vein failed to cure more than about 75 per cent of patients with varicose veins, and so in the years since the second world war stripping which was first practised by Mayo in 1906 was reintroduced in an improved form and is the standard method today,

fact to appreciate is that the venous drainage of this area of skin is not to the internal saphenous vein but passes via two or three perforating veins to the deep veins of the leg. In the case of the skin above the external malleolus the point is not so clearly made but nevertheless a large proportion of the venous blood from the skin of the lateral supramalleolar area passes directly to the deep venous system.

The second point is the relationship of venous ulcers to varicosities of the superficial veins. In my view Cockett paints a correct picture of the incidence of these two lesions when he gives the following figures; during a year 740 new cases of varicose veins without ulcer were seen and during a two-year period 182 patients were seen with venous ulcers; of these 182 patients 47 per cent had no obvious incompetence of the superficial veins, 22 per cent gave a definite history of an iliofemoral thrombosis or white leg, and in 11 patients the ulcer had recurred after an adequate high saphenous ligation.

The third point is the place of a previous deep venous thrombosis in the ætiology of venous ulceration. Statistics from a number of sources indicate that at least 45 per cent of patients with venous ulceration give a history of a previous deep venous thrombosis and that most patients develop their ulcer between two and five years after the deep venous occlusion.

Gryspeerdt and Cockett (1953) have used phlebography to study the state of the deep venous system in patients with venous ulceration. They find that in most patients with a previous history of deep venous thrombosis there is complete recanalization of the femoral and popliteal veins with destruction of the valves, but that in the other patients with exactly similar ulcers the deep veins are normal. They believe that this is evidence that some other factor must exist as a cause for this ulceration besides incompetence of the valves in the femoral and popliteal veins.

Another factor which favours the development of ulceration of the skin of the supramalleolar areas is the poor arterial blood supply of this region which may be an added reason why raised venous pressure in this area leads to ulceration, and venous pressure studies have shown that with exercise a high pressure builds up in the deep veins of the calf and when the valves on the perforating or communicating veins are incompetent this high pressure is transmitted to the small venules of the supramalleolar area.

These facts have led Cockett to postulate his theory that there must be a local fault to account for venous ulceration and in his view this local fault is incompetence of the ankle perforating veins, a condition which is made worse by associated incompetence of the internal and external saphenous veins.

The Ankle Perforating Veins. Two or three perforating veins pass from the region above the internal malleolus and carry the venous blood from this region directly to the posterior tibial veins. These veins pass through the deep fascia and each is protected by a valve near to its point of union with the posterior tibial vein. The superior perforating vein is the most constant in position and is situated on the inner side of the leg at the junction of its lower and middle thirds. It communicates with the internal saphenous vein by a small tributary and it is via this that the effects of internal saphenous incompetence can be transmitted to the supramalleolar or ulcer-bearing area. The middle perforating vein pursues a similar course, whilst the inferior or third perforating vein is a small inconstant and relatively unimportant vessel. The external perforating veins are usually two in number; the lower is a tributary of the external saphenous vein and passes directly through the deep fascia to join the peroneal vein, the upper is inconstant and unimportant.

saphenous vein. The external saphenous vein is now exposed where it lies behind and above the external malleolus. The stripper is then introduced and passed upwards to the popliteal incision. After a ligature has been tied round the vein and stripper at the ankle, the vein is divided at each end and the stripper pulled upwards and cut through the popliteal wound. Pressure and bandaging is applied as before and the wounds closed.

The ligature of incompetent communicating veins is usually performed for venous ulceration and the procedure will be described under that heading, but before concluding this section on the management of varicose veins, there are two further points which will be discussed. Varicose veins are common during pregnancy but they always at least partially regress after delivery. In our view the correct treatment of varices during pregnancy is support with an elastic stocking or bandage, operation being deferred until a few months after delivery. The second point is that many surgeons consider that a past history of thrombophlebitis or white leg contraindicates operations for varicose veins; this is not so if the tourniquet tests show that the deep veins have recanalized particularly with competent valves, although this latter point is not essential.

Ulceration of the Legs

(Anning, 1954, Dodd and Crockett, 1956)

Nearly all ulcers of the leg are of venous or arterial origin and therefore come under the heading of peripheral vascular diseases, but occasionally ulcers are seen from other causes and the most important of these will now be listed. Tuberculosis or syphilis may cause ulceration here as elsewhere, trophic ulcers occur in patients with tabes dorsalis or other neurological abnormalities, diphtheria may produce a diagnostic trap which once defeated me until the patient developed peripheral neuritis, blood diseases and, in particular, hæmolytic anæmia may cause ulceration of the legs, and there are a number of other causes including an underlying malignant tumour, the pyodermia which occurs in patients with ulcerative colitis, old poliomyelitis and erythrocyanosis frigida.

Arterial ulcers or the presence of an arterial element in a venous ulcer must always be suspected when the patient presents with an ulcer and other evidence of arterial insufficiency, but in our view it is rare to see ulceration of the legs of arterial origin cause difficulty in diagnosis because such ulceration is uncommon in the absence of well-established obliterative arterial disease and in most patients there is actual gangrene or rest pain as well. However, in some patients with a barely sufficient arterial supply, a minor injury may lead to ulceration, and it is in these patients and those with venous ulceration associated with arterial insufficiency that sympathectomy helps.

Venous Ulcers (Gravitational Ulcer) of the Legs. The term varicose ulcer should be abandoned because, as Gay stated in 1868 and as Anning (1949) and Cockett (1955) have so clearly shown, venous ulcers are, if anything, more common in patients without superficial varicose veins than with them.

ÆTIOLOGY

Cockett has reassessed the knowledge from the past and added fresh facts of his own so that he has been able to give a clear picture of the ætiology of venous ulcers which fits the facts as they are known today. Venous ulcers usually occur just above the internal malleolus or, less often, above the external malleolus, and the first and most important

told that they must avoid standing still for long periods but that exercise is beneficial and if they are forced to stand they should mark time frequently. It is also wise, particularly in the early stages, for them to sleep with the foot of the bed raised and when they sit in a chair to raise the bad leg on to another chair or a stool.

Operation

Ligature of the femoral or popliteal veins for venous ulceration is ineffective and best abandoned.

The internal and external saphenous veins should be treated in the manner already described if there is the slightest evidence of incompetence in either. Attention is then directed to the ankle perforating veins and here it is important to realize that there is some communication between the internal and external perforating veins; therefore in many patients it is wise to ligature both groups although an ulcer may be present on only one side of the leg.

Ligature of the Ankle Perforating Veins (Turner Warwick, 1931, Linton, 1952, Cockett, 1955). This operation may be carried out in one or two tissue planes—the extrafascial and the subfascial; the former is only suitable for early cases because skin necrosis may follow dissection in the subcutaneous plane, on the other hand an extensive dissection may be carried out in the subfascial plane without risk of impairment of wound healing.

The Extrafascial Operation. An incision is made about 1 in. behind the postero-medial border of the tibia from the middle of the shaft of this bone to about 1 in. behind and above the internal malleolus. Any large veins are dissected out until the perforating veins have been isolated as they pass through the deep fascia. Each perforating vein is then ligated with fine catgut and the wound closed. If there is a small ulcer this is excised and this portion of the wound left open, a split skin graft being applied four or five days later.

In many patients it is wise to proceed at once to expose and divide the lateral ankle perforating vein or veins. An incision about 4 in. long is made just lateral to the line of the outer border of the tendo achillis, its lower end being about 4 in. above the tip of the external malleolus; as before any large veins are followed until the perforating vein has been found and tied.

Subfascial Operation. This is reserved for patients with severe ulceration and induration, and so a period of pre-operative preparation with bandaging to reduce swelling and infection is important. The incision is similar to that used for the extrafascial operation but it may be made a little larger at the upper end, and the ulcer is excised. It is carried straight through the deep fascia and the dissection carried out deep to that layer. The medial perforating veins are then tied and it is possible with retraction to tie the lateral perforating vein through the same incision. The skin is then closed with great care and the ulcer area grafted as before on the fourth or fifth post-operative day. The danger of these operations is the possibility of skin necrosis but efficient pre-operative preparation, meticulous technique and the use of the subfascial approach in most cases will reduce the incidence of this complication to a minimum.

The post-operative management consists of firm bandaging, elevation of the foot of the bed and active toe, foot, ankle, and knee movements to prevent venous stasis and thromboembolism. The patient may get up about one week after the skin graft has been

In many patients with a femoral or popliteal venous thrombosis the occlusion involves these perforating veins, particularly those on the medial side. When these recanalize they are valveless and the stage is set for venous ulceration. But what is almost more important is that the thrombosis in the veins of the calf muscles which is a relatively common condition and which may pass unnoticed may spread and involve these perforating veins with similar results.

At operation it is possible to tell whether these perforating veins have competent or incompetent valves by a simple test devised by Turner Warwick (1931). When a perforating vein is divided it does not bleed if it is normal but it bleeds a little if a probe is passed up it to disturb the valve. On the other hand, if the valves are incompetent steady bleeding occurs.

Clinical Picture

The ulcer is situated just above the medial or lateral malleoli but may in severe cases grow so large that it encircles the limb. They are seen more frequently in women than men and there is usually distension of the venules in the area with eczema, induration, œdema, pigmentation, and pain. In severe and long-standing cases there is contracture of the calf muscles with shortening of the tendo achillis and an equinus deformity of the ankle. Venous ulcers have one important clinical characteristic: whatever their size complete bed rest with elevation of the foot of the bed will cause them to heal if prolonged for a sufficient length of time, but if the cause has not been removed they relapse rapidly when the patient gets up.

The actual appearance of the ulcer will vary with the degree of infection and its chronicity, but they have a sloping edge and a granulation tissue base. They may be fixed to the underlying periosteum and the tissues around show distension of the venules, induration, œdema, eczema, pigmentation and perhaps scarring where a previous ulcer has healed. As with peptic ulcers, the problem is not so much how to heal the ulcer but how to keep it healed. Very occasionally an epithelioma develops in the edge of a long-standing ulcer; any suspicious area should be biopsied.

Treatment. The prophylactic aspects of this will be discussed in the section on thrombophlebitis. Here the management of the established ulcer will receive attention.

As stated, these ulcers heal if the local venous hypertension is relieved by bed rest but they relapse rapidly. On the other hand, efficient and prolonged elastic support with an elastic pressure or adhesive bandage will, as Dickson Wright (1930) has shown, heal these ulcers, and if maintained afterwards a relapse will be prevented. The first essential is to refrain from applying all but the most bland and simple preparations to the ulcer itself; antibiotics, antiseptics and other preparations designed to reduce infection should be avoided because of the risk of sensitivity reactions. The infection will subside with efficient bandaging. The bandage or adhesive elastic strapping must be applied from the toes to the knee and cover the whole limb between these points; it should be applied with the greatest care to get smooth even compression, and extra pressure to the ulcer may be obtained by incorporating a felt pad in the bandage. At first attendances should be frequent but as the discharge gets less and the ulcer gets smaller the attendances may get less and less frequent because the patient may take over more and more the bandaging of his own leg. After the ulcer has healed the patient should continue wearing an elastic bandage or efficient elastic stocking for years or the rest of his life. Patients should be

Thrombophlebitis Migrans. In this condition venous thrombosis occurs first at one place and then at another, either with a short interval between attacks or the patient may be symptom-free for long periods. In many patients no cause is found but in men below 40 years of age thromboangiitis obliterans should be taken to be the likely cause until proof to the contrary has been obtained. The treatment of a single episode or episodes occurring with a wide time interval may be the same as for thrombosis in a varicose vein, but if attacks are frequent long-term anticoagulant therapy may be instituted.

Ilio-femoral and Calf Vein Thrombosis. Phlebothrombosis of the calf veins leading to thrombophlebitis and later ilio-femoral thrombophlebitis is a fairly common complication of bed rest, particularly after coronary occlusion, major respiratory tract infections, a surgical operation or parturition. Murley (1950) found a 9 per cent incidence of leg vein thrombosis in a series of cases carefully examined for this condition.

Clinically the first signs may be tenderness in the calf, a mild pyrexia and a positive Homan's sign, or a pulmonary embolus may occur before any abnormal clinical features are noticed in the lower limbs. Later the leg may become swollen and the full picture of ilio-femoral thrombosis become established.

Ætiology

The exact reasons why a patient may develop this condition are not known but certain factors appear to predispose towards the clotting of the blood in the calf veins; amongst these may be included: venous stasis, infections, malignancy, old age, local or general trauma and perhaps local changes in the blood.

Treatment. Efficient prophylactic measures can prevent the occurrence of this condition in many patients. These include gentleness during surgical procedures, the avoidance of positions which interfere with the venous return from the lower limbs, toe, foot, ankle, and knee exercises for medical as well as surgical patients both before and after operation, early ambulation, and in patients in whom the condition is thought to be likely prophylactic anticoagulant therapy.

Once established the condition should be treated by bed rest, elevation of the lower limbs, the continuance of toe, foot, and ankle exercises and anticoagulants. Two other measures are in fairly general use and these, para-vertebral block and venous ligation, will be discussed individually.

Paravertebral Block with novocaine—this is unsafe if a full anticoagulant regime has been established, but before this it is a worthwhile procedure in the acute stage of the disease if the limb is painful, swollen, and white.

Venous Ligation—there is no doubt that this procedure was practised too frequently but it has a place in the prevention of pulmonary embolism under certain conditions. An obvious indication is septic thrombophlebitis, another is a pulmonary embolus in the preoperative period when the operation itself cannot be postponed, and a third is in a patient who has recurrent pulmonary emboli in spite of adequate conservative measures. An essential feature for the success of the operation is that the ligature should be placed proximal to all the clot. This means that routine ligation at any one level is impossible; in some patients it may be the superficial femoral vein, in others the common femoral and occasionally it may be necessary to tie the inferior vena cava.

It is important to realize that treatment must not stop with the passage of the acute phase and the removal of the risk of pulmonary embolism. Whilst still in bed and during

applied but a firm elastic bandage is essential until the area is soundly healed. After this many patients require an elastic stocking.

Some surgeons have advised lumbar ganglionectomy as an additional aid towards the healing of venous ulcers. In our view it is only indicated when there is evidence of arterial insufficiency as well as the venous abnormality. It will be appreciated that these operations are by no means minor in nature, but venous ulceration is a major disability causing much incapacity and loss of working efficiency, therefore a procedure such as this which raises the earning capacity of the patient is well worth the time and trouble entailed.

Thrombophlebitis, Phlebothrombosis and Venous Embolism

This may affect the superficial or deep veins. As the name implies, thrombophlebitis is an inflammatory lesion in which the vein thromboses and the lesion may be associated with a demonstrable infection or the inflammation may be sterile. The septic variety of thrombophlebitis is rare and may follow an infected lesion or faulty technique in performing such a minor procedure as the injection of varicose veins. In the past this was a very serious event but today antibiotics combined with proximal ligation of the appropriate vein have reduced the mortality. Phlebothrombosis is the clotting of blood within a vein without any evidence of inflammation and in many patients the condition of phlebothrombosis progresses rapidly to thrombophlebitis. The important difference between the two conditions is that the clot in phlebothrombosis is not adherent and in fact it often lies free in the lumen of a vein with the blood flowing past in an apparently normal manner, whilst in thrombophlebitis the clot is adherent to the wall of the vein; this means that phlebothrombosis is a far more serious condition because the risk of pulmonary embolism is much greater.

Thrombophlebitis in Varicose Veins. This is a common occurrence and may be caused by a minor injury. The patient complains of pain and tenderness in the region of the thrombosed vein. Upon examination the vein is palpable as a tender cord, the surrounding tissues are œdematous and the overlying skin reddened. The signs of inflammation soon disappear but the vein remains palpable as a firm cord for some months.

In most patients thrombosis in a varicose vein is an innocuous condition and support with a crepe or elastic bandage is all that is required, but as Martin and his colleagues (1956) have pointed out the patient in whom the thrombus has reached the upper thigh must be treated more energetically. In these patients it is wise to expose the saphenofemoral junction and open the saphenous vein before tying it. In many such patients a tail of clot will be found extending into the common femoral vein and operative intervention will prevent the occurrence of a pulmonary embolus from this zone of phlebothrombosis which has become superimposed on the area of thrombophlebitis below.

Thrombophlebitis after Intravenous Therapy. A simple intravenous injection, an intravenous anæsthetic or an intravenous infusion may be followed by thrombosis of the vein concerned. Meticulous technique will reduce the occurrence of these complications but those occurring particularly after an intravenous infusion require active treatment. The infusion should be stopped and the needle or catheter removed, antibiotics should be given in full dosage because of the occasional occurrence of septic thrombophlebitis in such patients. The part should be placed at rest, elevated and local heat (antiphlogistine) applied. If, in spite of this, the clot appears to be spreading anticoagulants should be prescribed.

most likely explanation is that of Kinmonth (1954), he thinks that the cause in some cases is dilatation of the iliac lymph trunks producing an incompetence similar to that of a valveless ilio-femoral vein, and he suggests that the condition might be relieved by ligating these incompetent lymph trunks.

The onset is usually in the second decade and usually a girl. The lower leg and ankle swell first, later the foot and thigh. In most patients the condition is unilateral. At first the condition disappears each night, later prolonged bed rest is required to return the limb to normal, and finally the œdema ceases to pit and does not disappear with elevation. The overlying skin now becomes thickened and infection is common.

Treatment. These patients always consult a doctor during the early stages of their disease when the œdema can be made to disappear with elevation. If the condition is recognized as the serious condition it is, adequate treatment at this early stage can prevent much trouble later on. The patient must sleep with the foot of the bed raised and control of the swelling throughout his working hours with an elastic bandage or an Unna's paste bandage; unfortunately elastic stockings tend to lose their efficiency so quickly that they are often ineffective in this condition unless they are renewed regularly. The patient will have to be told that he may have to continue this regime for life but that the trouble is worth it because of the state of affairs it prevents.

If the disease has progressed to the stage of non-pitting œdema, then compression bandaging and elevation can at the best produce improvement only for these patients; surgery must be considered. A variety of methods have been designed by such surgeons as Handley (1908), Kondoleon (1912), Gillies (1925) and Fraser (1935) to re-establish the lymphatic drainage and have been tried but they are ineffective. The only satisfactory procedure is to excise the subcutaneous tissues; an unsightly but useful leg is the result of such an operation efficiently performed (Mowlem, 1948).

Congenital Lymphœdema
(Milroy's Disease)

The term Milroy's disease (1892) should be reserved for the hereditary form of congenital lymphœdema. Congenital lymphœdema may involve part or the whole of one or more extremities. The exact cause is not known but in a proportion the condition may be a true lymphangioma, particularly when the abnormality is localized to part of a limb; in others the cause is probably an interference with the lymph flow of one of the types already mentioned. The condition is uncommon and true Milroy's disease is a rarity.

Clinically Milroy's disease is a pitting œdema of one or more limbs present at birth. The œdema soon ceases to pit and the limb becomes firm and indurated. Characteristically the œdema stops at the groin or knee or some other anatomical boundary and does not spread beyond this level in the way that lymphœdema præcox or spontaneous lymphœdema can spread up a limb.

The localized form of congenital lymphœdema presents a different picture. Part of a limb is swollen and the swelling does not pit on pressure. The swelling has an ill-defined but none the less recognizable edge and increases in size with the passage of years. Later, on the overlying skin blisters appear and these burst and discharge lymph; as a rule this lymph discharge rapidly ceases but in some patients a true LYMPH FISTULA results. This interesting and unusual lesion consists of the discharge from an almost

the acute phase the limb should be firmly bandaged from the toes to the groin. This firm bandage must be continued when he gets up until all trace of œdema or swelling has disappeared; an elastic bandage should be used and if the swelling persists the patient should continue with this or an efficient elastic stocking after discharge from hospital. Failure to provide efficient support leads to the post-phlebitic syndrome and venous ulceration.

Thrombosis of Either Vena Cava. Thrombosis of the inferior vena cava is usually due to extension from the iliac veins, although it may occur as a result of pressure by a tumour or aneurysm. On the other hand, thrombosis of the superior vena cava is usually due to a tumour but may occur as a result of the rare condition of superior mediastinal fibrosis or from other causes such as thrombophlebitis. In each case there is swelling and œdema of the parts distal to the obstruction, venous engagement, cyanosis and the presence of enlarged veins where the collateral circulation is being established. Treatment is along the lines already described after a careful study has been made to exclude a removable tumour as the cause.

Thrombosis of the Axillary and Subclavian Veins (Hughes, 1948). This may arise as part of the thoracic outlet syndrome but more often there is no obvious cause apart from a history of some unusual activity; two of our patients, both men in sedentary occupations, developed the condition after distempering a ceiling. In some patients with the fully-established clinical syndrome operation has shown that the vein is patent. The condition causes œdema, swelling, cyanosis, venous engorgement and a feeling of heaviness, but no pain. Treatment is by elevation, rest, physiotherapy, anticoagulants, and in severe cases sympathetic nerve block with novocaine.

DISEASES OF LYMPHATICS

Diseases of Lymphatics. The lymphatic system is the least well understood of the three major parts of the vascular system and, as lymphangiography and lymphangiomas have already been discussed, this will be a short section.

Lymphœdema. The circulation of lymph in man may be studied in a variety of ways including lymphangiography (Kinmonth, 1954), the injection of patent blue (Kinmonth, 1954), an analysis of the tissue fluid (Boyd, 1950), a study of the pressure of the tissue fluid (Wells, Youmans, and Miller, 1938) and the absorption rate of radioactive protein (Kinmonth and Taylor, 1954).

Lymphœdema may be defined as œdema due to lymphatic obstruction but in clinical practice it is often impossible to be certain that this is the only cause. There may be venous œdema as well, and in our view the statement which is sometimes made that lymphœdema does not pit is incorrect; in its early stages at any rate it pits. Lymphœdema has one point which distinguishes it from venous œdema—ulceration does not occur.

Lymphœdema Præcox or Spontaneous Lymphœdema

Lymphœdema præcox or spontaneous lymphœdema may be defined as lymphœdema of unknown cause, developing for the first time early in life. There are three possibilities to account for at least some of the cases of lymphœdema præcox; these are simple lymphatic obstruction, but here the difficulty is that lymphœdema rarely develops after the most extensive groin dissections for carcinoma; the second is that there is a connection between the intestinal lymphatics and those of the lower limb; and the third and

Post Traumatic Lymphœdema

Œdema may follow any injury and is particularly likely to occur in a limb which has been immobilized in plaster of Paris when the plaster is removed. This œdema is probably of both venous and lymphatic origin but a pure lymphœdema may occur after an injury. A peculiar abnormality of this type is the LYMPH CYST which may occur after a fracture; the two examples of this abnormality which we have seen both followed fractures of a long bone. One patient suffered a fracture of the upper third of the shaft of the fibula; at first all went well, then the leg became painful and a subcutaneous swelling developed over the site of the fracture, the swelling contained about 150 ml. of lymph and, although aspiration was repeated on many occasions and a compression bandage applied, the size of the cyst increased rather than decreased in size. Excision of the cyst did not affect a cure presumably because it was incomplete but later it became infected and drainage became necessary; the wound healed, the discharge ceased and the cyst has not recurred.

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invisible point on the skin usually of the thigh or groin of a large quantity of lymph, the discharge persists for days or weeks and then stops but after an interval it starts again and the process is repeated. In such patients one can usually palpate in the region of the fistula an area of thickening and induration. In one of our patients G. W. Taylor of St. Bartholomew's Hospital was able to demonstrate dilatation and incompetence of the iliac lymph vessels; interruption of these has at least produced a temporary improvement. This patient was a boy aged 8, the lesion was on his left thigh and had been present since birth. Every few weeks he discharged about 2 litres of lymph from a very small sinus on the part of the middle of the thigh and was then symptom-free until the next attack. The only other patient we have seen with this type of lymph fistula was aged 41, the fistula had been present for as long as he could remember; the history was similar to that for the boy and it caused him little inconvenience, during attacks he wore an absorbent dressing and there was no history that infection had ever occurred.

Differential Diagnosis of Congenital Lymphœdema. It is possible to confuse the enlargement of a limb which occurs in patients with congenital arterio-venous fistulæ with congenital lymphœdema, but the limb with an arterio-venous fistula rarely presents with a true pitting œdema, there is instead a generalized enlargement as regards both girth and length. LIPŒDEMA is a curious condition in which there is œdema but in which the main increase in size is due to the deposition of large amounts of fat. It may develop during infancy and childhood or be present at birth. The swelling does not usually pit and the patient may suffer from repeated attacks of pain due to fat necrosis. CONGENITAL NEUROFIBROMATOSIS may cause occasional difficulty but the swelling here, although being apparently diffuse, is in fact nodular on palpation.

Treatment of congenital lymphœdema is on the lines already laid down for lymphœdema præcox

Secondary Lymphœdema

Lymphœdema may arise secondarily as a result of a variety of causes including: recurrent inflammation, infiltration with malignant disease, after treatment with a combination of radiotherapy and surgery, or surgery alone, after an injury, as a result of filariasis, as a result of an allergic reaction, and as lymphœdema artefacta.

Of these the most important are those associated with malignant disease and particularly the BIG ARM which develops after treatment of a malignant breast tumour. This œdema which develops in the arm may be of mixed venous and lymphatic origin, may be due to infiltration with tumour tissue, surgical ablation of the lymph or blood vessels, radiotherapy, or a combination of all these processes. The swelling may be localized as, for example, to the back of the distal half of the arm just above the elbow or the whole limb may be involved. Treatment is difficult and in the main consists of elevation when possible, physiotherapy and pressure bandaging.

Inflammatory Lymphœdema

Some think that recurrent attacks of inflammation particularly with streptococci are the cause of this condition; others think that the lymphœdematous limb is very much more likely to suffer from recurrent attacks of inflammation, that such inflammation may make the lymphœdema worse but that it is rarely, if ever, the primary cause. In all patients with swollen and œdematous limbs infection must be treated energetically and, if possible, prevented.

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Tissue Reconstruction. In reconstructive surgery diagnosis is mainly concerned with an exact analysis of the existing or latent defect. The surgeon must define both the extent of the deficiency and what tissues are involved.

It is an established principle that tissue defects should be repaired, if possible, by new tissue of the appropriate kind: that is, skin losses require new skin, and defects of bone require a bone graft. There are however, certain exceptions and these will be discussed in their proper context; but it may be noted that technical difficulties curtail the use of both mucosal and cartilage grafts.

The replacement of skin should always be considered primarily from a functional rather than a cosmetic standpoint. The skin is an elastic envelope and its integrity is essential to the health of the body, and particularly to the equilibrium of what Claude Bernard called the "milieu intérieur." Retention of body fluids is of course essential to life, and consideration of the serious consequences of fluid and electrolyte loss from burns indicates the complex but vital nature of this function.

However, the skin is also concerned in the whole range of body movements, especially of the face and limbs, as well as in certain other physical activities; and function is of outstanding importance in the reconstruction of all areas which are involved in movement. A band of scar in the axilla, a loss of skin below the eye causing ectropion, or a fractured nose with obstructed airways are obvious examples of lesions which are essentially functional—and only incidentally cosmetic—in their ill-effects.

Tagliacozzi put the principles of plastic repair in their proper perspective three and a half centuries ago when he wrote: "We bring back, refashion and restore to wholeness the features which nature gave but chance destroyed . . . and the end for which the physician is working is that the features should fulfil their offices according to nature's decree."

PRINCIPLES OF SKIN REPLACEMENT

Skin defects may be repaired by a number of methods, which should always be considered in the following order:

Local Skin Flaps

In principle this technique involves redistribution of local skin, depending on spare skin from adjacent areas, or on the natural elasticity of the skin which allows alterations in tension. Local skin flaps may also be moved at the expense of a secondary defect which will require grafting. Local repair follows one of the following designs (Fig. 81).

Sliding Flaps. These involve the mobilization of the marginal skin, and are ideally adapted to closing an elliptical defect. Lateral relaxation sutures should never be used in the hope of relieving tension.

Advancement Flaps. The "advancement" of a flap implies the movement of an area of skin, often in the form of a triangle or rectangle, in a direct line away from its base. In its pure form it has few applications, apart from the well-known V-Y advancement and certain neck flaps.

Rotation Flaps. These have a wide application, and are extremely versatile in many sites. The apex of the flap is moved through an arc, the radius of which is roughly equivalent to the length of the flap, and the centre of which lies near the base. Frequently the secondary defect is self-closing, that is to say there is a redistribution of skin and no

CHAPTER III

PLASTIC SURGERY

C. R. McLaughlin

GENERAL PRINCIPLES

The Scope of Plastic Surgery

Reconstructive surgery is in some respects a young science which has only attained the status of a separate specialty in this country since 1916. At this stage it is difficult to give a succinct and comprehensive definition of its precise scope. In brief, it is concerned with the restoration of normal form and function over most of the body surface, and it is important that the functional aspect should never be over-shadowed by the cosmetic. It is related first and foremost to the provision of satisfactory skin cover for the patient, whether his defect is due to a congenital, pathological, or traumatic lesion. It is also concerned with the contour of the face and, in special circumstances, of other parts of the body. Finally plastic surgery may be applied to lesions of certain body cavities, including the mouth and pharynx, eye socket, urethra and vagina.

Historical

There are records of attempts at reconstructive surgery extending back through 35 centuries. In the Edwin Smith Papyrus, which scholars estimate to have been written before B.C. 1600, a number of "plastic" problems are discussed, and it includes an accurate description of the modern method of reducing a dislocated jaw. The first well-documented references to skin reconstruction in Europe date from the fifteenth century, though it is likely that these methods had previously come from India. Fioravanti gives a most circumstantial account of a free graft carried out in dramatic circumstances in 1551; a portion of nasal skin, which had been sliced off during a duel and had fallen on the sand, was successfully replaced; he records that the graft survived permanently.

In 1597 the first great textbook of plastic surgery, "De Curtorum Chirurgia," was written by Gaspare Tagliacozzi. It is difficult to exaggerate the importance of this publication, or the genius of its author. It is sufficient to mention that he came close to discovering the tubed pedicle 320 years before its time, and that his method of reconstructing the nose from the upper arm still gives admirable results.

Free skin grafting made little clinical progress until Reverdin (1869) used epidermal pinch grafts successfully. Ollier of Lyons and Thiersch in Germany were responsible for advances in grafting larger sheets of skin during the next decade, and a German emigrant, Wolfe, working as an oculist in Glasgow, gave his name to the full thickness skin graft in 1875.

Apart from some interesting observations by McEwan on bone grafting, little progress was made in this country until the urgent stimulus of the first World War fired the genius of Gillies and his colleagues, and produced the remarkable renaissance of reconstructive work which still continues.

free graft is necessary. These flaps are particularly applicable to the skull, where the skin is inelastic and it is impossible to "steal" tissue.

A special type of rotation flap is associated with the name of Imre, and is in fact a combined advancement-rotation flap. The axis of movement follows an arc with a relatively long radius and distant centre. Or to put it in different terms, one margin of the

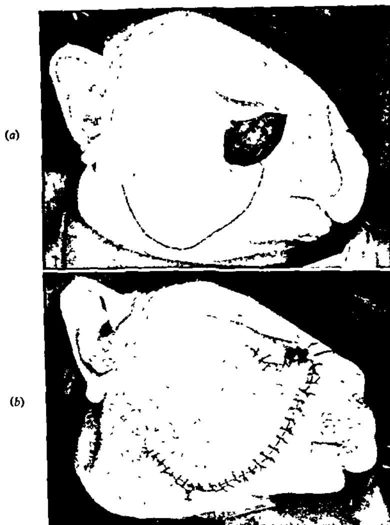


FIG 82. (a) Defect following excision of carcinoma involving left lower lid.
(b) Repair by rotation-advancement (Imre) flap.

flap advances nearly in a straight line, while the other margin is rotated. The general effect is that the flap acts in the nature of a wedge, and it can be used to good advantage below the lower eyelid when there is a skin shortage in a vertical direction (Fig. 82).

Transposition Flaps (Single). Transposition of a skin flap implies that it is raised and moved across intervening and intact skin to a new position. A number of special designs are included in this category. Important examples are the forehead flap, which is used for rhinoplasty; the full thickness flap of the lips as described by Abbe and Estlander (q.v.); and the "fan" flap of Gillies, where a full thickness flap is transposed from cheek to lip.

Transposition Flaps (Double). This device of using two similar flaps (designed approximately as equilateral triangles) is known as a Z-plasty. It has many applications in the release of linear tension, particularly if there is a skin web. When the two flaps are

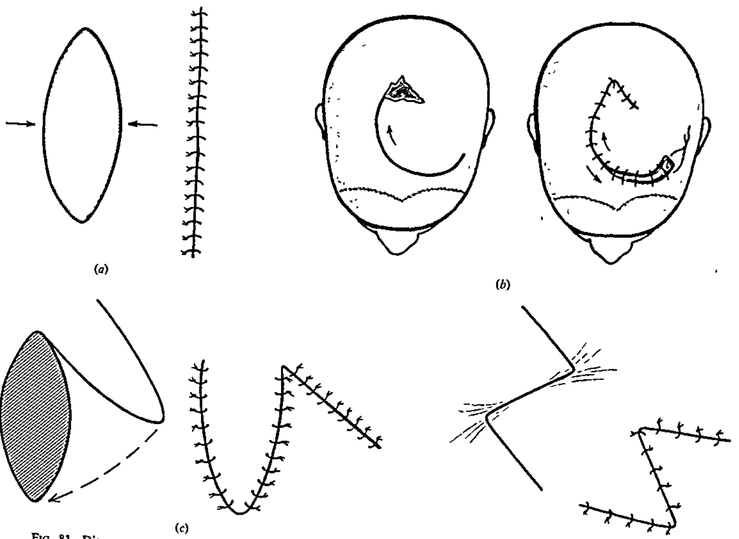


FIG 81. Diagrams to show (*a*) sliding flaps, (*b*) rotation flap, (*c*) transposition flap, and (*d*) double transposition flaps.

Indirect flaps are carried from one site to another via one or more points of secondary attachment. Commonly the wrist is used as a carrier.

Sometimes these flaps are used in the form of tubed pedicles, but the principle of migration is the same.

Tubed Pedicles. This device, one of the most spectacular and versatile in plastic surgery, was discovered independently in 1917 by Filatov in Russia and Gillies in Britain. It has the enormous advantage that the under surface of the flap is closed without secondary grafting; this encourages a rich longitudinal blood supply, which remains active throughout all stages of migration. It is, however, a manœuvre which, though simple to begin, is not always so easy to conclude satisfactorily. Its application to the lower limb, which might appear to hold many advantages, is fraught with particular hazard.

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General Principles

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TECHNICAL ASPECTS OF SKIN REPLACEMENT

GENERAL TECHNIQUE

An appreciation of the operative standards necessary for success in skin reconstruction should not be confined to plastic surgeons. It is, however, difficult to generalize either on the proper mental approach or on technical minutiæ and special instruments.

The manipulation of delicate tissues must always be conducted with delicacy of touch aided by atraumatic instruments. An atmosphere of gentleness, precision and unhurried concentration is essential. The surgeon and his assistants should be seated whenever possible. This encourages a steadier technique and prevents manual fatigue. The classical position described by Rose for lip surgery can be adopted with advantage for almost all facial operations, except where the patient is in the tilted position. The Rose position, where the patient's head is virtually in the surgeon's lap, gives him a close and almost vertical view. However, in certain cases, especially where hypotensive anæsthesia with postural ischæmia is indicated, the surgeon must stand at the patient's shoulder and make the best use of the tilt.

As regards lighting, a single lamp in exactly the right position is often preferable to a variety of spot lights, but the latter type may occasionally be needed. The important point is that the beam should strike the operative field at the optimum angle, which is usually a right angle.

mutually transposed there is a considerable gain in one axis, and in theory this linear increase may be as much as 70 per cent.

Other Examples. Advantage may sometimes be taken of a known artery entering a skin flap. With this assured blood supply, long narrow flaps can be designed. They are known as "arterial" flaps, and were originally described by Esser.

"Island" flaps are those where a skin area, exactly measured to fit an established defect, is moved on a subcutaneous vascular pedicle. This neat device has only infrequent uses.

Free Skin Grafts

Skin Autografts. Skin grafts are usually classified according to their thickness, and this is a convenient system.

(*a*) *Full thickness skin grafts* (*Wolfe*) are much superior to thinner grafts in terms of appearance and absence of contracture. In most areas the secondary defect is apt to require secondary grafting. The ideal donor tissue for small areas is the post-auricular skin.

(*b*) *Split skin grafts* include the epidermis and part of the dermis; they are sometimes called dermo-epidermal grafts. For convenience they may be considered as thick or thin skin grafts. The thick variety includes the "three-quarter thickness" graft obtained by the dermatome. Thin grafts, which are loosely called Thiersch grafts, are mainly epidermal but include some dermis. They offer the best prospect of a good "take" on a granulating surface, but they undergo greater contracture than Wolfe grafts. Split skin grafts may in certain circumstances be applied as small rectangles called "postage stamp" grafts. The only advantage of this technique is a certain economy of tissue, but it is bound to involve delayed healing with scar formation.

(*c*) *Intermediate skin grafts* include the modified type of pinch graft described by Staige Davis. The centre of each graft includes the whole dermis, the graft tapering sharply towards the periphery which is extremely thin.

Skin Homografts. The term homograft is used of grafts taken from other members of the same species (as opposed to heterografts which are from different species). Human homografts have a limited clinical application, as they invariably degenerate and disappear within two months, except in the case of identical twins.

In spite of intensive and invaluable clinical and experimental research, notably by Medawar, no solution has yet been found to this problem; even the exact mechanism is still disputed. Consequently there has been little clinical progress, and homografts at present have few applications. However, they are useful in severe burns, especially in children, where the patient's donor areas are limited It has been found effective, by Mowlem and others, to apply the homografts in strips alternating with autografts. In this way epithelium from the autografts has a chance of extending fast enough to replace the degenerating homografts.

Transferred Skin Flaps

Skin defects may be repaired by full thickness skin flaps transferred from parts of the body not adjacent to the lesion. These are of two kinds: (*a*) direct, and (*b*) indirect.

Direct flaps are those which are carried in a single transfer from one site to another. They include cross-leg flaps, cross-finger flaps, direct flaps from the abdomen to arm, and many other varieties.

"Vertical" mattress sutures are useful to prevent inversion of edges, but must not be tied tightly. Knots in general should be tied with instruments and not with fingers. Sub-cuticular sutures have a limited sphere of usefulness. They are well suited to the upper eyelid, where their correct insertion is a good test of manual and visual co-ordination. Sub-cuticular wire may be used to close forehead and neck wounds, where ordinary sutures are apt to leave marks. Buried catgut sutures should be used with discretion; they are indicated where the wound involves a definite deep layer such as fascia or platysma. They should never be used in the dermis to reinforce skin closure.

Dressings are an important part of good technique. Clean suture lines should never be covered with tulle gras or other greasy dressings. Dry gauze is suitable, but some surgeons prefer the gauze to be moistened, as this encourages a degree of moulding so that the dressing fits the local contours closely. In any case a moist dressing soon becomes dry, so there is no risk of maceration.

Tulle gras is used to cover free grafts, while moist gauze, or wool impregnated with flavine and paraffin, is applied outside it. Raw areas which are being prepared for grafting may be dressed in one of several ways; either every 4 hours with Eusol or saline, or daily with a mixture (in equal quantities) of Eusol and paraffin, or with gauze soaked in an aqueous solution of streptomycin (1 gram per 100 c.c.s) and covered with jaconet as suggested by Kilner and others. This latter method is an excellent way of using an antibiotic for a limited time prior to grafting, so that organisms are not able to develop resistance. There are, of course, many other satisfactory methods.

All dressings are protected by a generous layer of cotton wool, and a crêpe bandage is recommended, unless elastoplast is preferred in certain cases.

LOCAL SKIN FLAPS

The skin over most of the body is elastic, though in varying degree. Apart from its intrinsic capacity to stretch, it is also mobile and can thus be moved within limits in relation to deeper structures. Both these characteristics depend on many factors, but mainly on site and age. The scalp is inelastic and relatively immobile; by contrast the skin of the neck, especially in the aged, is remarkably adaptable.

Though a large flap tends to be less vulnerable than a very small one, the question of shape is much more significant. The important point is the ratio of length (base to apex) compared with breadth. It is usually taught that this ratio should in general not exceed 1·5 to 1, but there are many exceptions, particularly on the face.

The difficult question of the local blood-supply must now be considered. There are no exact rules or mathematical criteria to guide the surgeon in assessing this vital issue. Though it may ultimately be a matter of experience and even common sense, certain points should be appreciated.

(1) The venous outflow through the base of the flap is as least as important as the arterial inflow.

(2) The normal vascularity of certain areas is notoriously poor—e.g. the ankle; and in other sites the vascular pattern may be unfavourable, as in crossing the midline of the abdomen.

(3) Very thin tissues like the eyelids, though highly vascular, are extremely susceptible to injury by careless handling.

It should be pointed out that, whereas thick flaps may carry much fat, which in terms

Instruments must be well chosen, though a large selection is seldom necessary. They should be light in weight, and conform in general to the standards appropriate to brain surgery; for example, skin hooks (as used for the dura) and Adson's dissecting forceps are invaluable. A well-designed sucker is constantly required, and the negative pressure produced by the suction machine should be capable of variation.

Sutures should be of the lightest calibre consistent with safety; fine plain catgut, waxed black silk and gossamer silkworm gut are the materials which are most used. Nylon is not well suited to this branch of surgery.

Operative Methods. The use of a sterile pen and Bonney's blue ink is a necessary part of reconstructive operations. The area to be excised must be exactly defined whether it is a malignant ulcer or the margin of a cleft lip; also all skin flaps should be marked before being cut; and in unusual cases a provisional plan can be tried out and assessed graphically, prior to operation.



Fig. 83. Lines of choice for facial incisions They also indicate the best axis for various elliptical excisions.

Incisions must be carefully planned. In nearly every elective operation it is possible to follow the lines of skin tension closely. In older patients these lines are obvious in the form of skin creases. In the young a very close examination will give some indication of the best line, as judged by the direction of tiny wrinkles or lanugo hairs. However, there is a general pattern common to most individual patients and this should be recognized. A few well-known examples may be quoted very briefly, relating the part to the direction of choice: Upper lip, vertical; lower lip, horizontal; medial part of the cheek, nasolabial groove; cheek in front of ear, vertical and very close to tragus; lower lid, parallel and close to lid margin; upper lid, horizontal; forehead, horizontal; upper neck, parallel to, and just below, the line of the mandibular branch of facial nerve (Fig. 83).

If possible skin should be cut in such a way that the blood flows away from the knife; incisions must always be at right angles to the plane of the skin; bevelled edges are unsatisfactory to suture. The undermining of skin is usually begun with a knife, the blade being held flat; at the same time the skin edge is held up under steady tension by marginal hooks. Extensive undermining may be completed with curved scissors, the main requirement being to keep in the proper plane of separation.

Most wounds are best closed by simple sutures; considerable practice however is needed to insert these to the best advantage. The needle must enter the skin, close to the edge, vertically; and it must emerge vertically on the other side. Thus the suture when tied will lie in the form of a square (as seen from the side), rather than in a circle. Each suture should take only a small "bite" of skin, say 2–3 mm. They must be inserted in a uniform and regular pattern; on the face eight sutures to the inch may be necessary.

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(3) Very thin tissues like the eyelids, though highly vascular, are extremely susceptible to injury by careless handling.

It should be pointed out that, whereas thick flaps may carry much fat, which in terms

of blood supply is parasitic, very thin flaps are easily bruised and may suffer marginal thrombosis. The important subdermal vascular plexus lies in immediate contact with the under surface of the dermis, but clumsy or excessive thinning of a flap can still cause unseen damage with dire results.

The safest design is the arterial flap described by Esser. These flaps are based on a known artery—for example, the superficial temporal—and in selected cases they may be designed with a length/breadth ratio of 6 to 1. Unfortunately they cannot often be used thus; but they emphasize the principle of making the best use of the precise anatomical pattern of the adjacent vessels.

The first rule of skin-flap surgery is "*Avoid tension.*" It is tension which causes ischæmia, kinks the base and retards the venous return, makes sutures cut out, and results in permanent distortion. The whole aim of the operator should be towards so disposing the tissues that the flap lies naturally, without either causing or suffering distortion.

Flap operations do not create new skin; they simply shift it to suit exigencies of the situation. If there is no skin "reservoir" at hand, a secondary defect may result, and this must always be grafted.

The handling of vulnerable skin flaps demands not so much special methods as special standards. Surgeons do not generally treat the abdominal skin edges with the same meticulous care that they reserve for a gastric anastomosis. But any surgeon who attempts reconstruction with skin flaps must exercise a degree of gentleness usually associated with eye surgery. Fine skin hooks, sharp needles, silk sutures of minimal calibre, and the avoidance of all crushing and dragging of the skin margins—these are the simple but imperative requirements of plastic surgery.

FREE GRAFTS

Full Thickness Grafts (Wolfe)

Although full thickness grafts may be cut from any convenient part of the body, the most favourable sites are near the clavicle, and behind the ear. Post-auricular skin is ideal in quality, its only disadvantage being the limited area available. A piece of jaconet or silver paper is cut to the exact shape of the defect, and this is laid over the skin with the ear held forwards in such a way that the raw areas over the mastoid and the ear approximately match, and the defect can be closed by direct suture. The graft is cut with a knife, keeping the plane of dissection as close as possible to the skin. The graft is then carefully cleared of any vestiges of fat or connective tissue, and sewn into position. A few of these sutures are left with one end long, and these ends are tied over wool impregnated with flavine and paraffin emulsion, or some other suitable dressing. The graft can be safely left for 5 days, but it is noteworthy that if it is necessary to examine the graft at an earlier stage, there may be a visible blood supply after 24 hours.

The presence of an early blood supply is extremely important, and has not always been widely recognized. It does in fact occur with all successful Wolfe grafts, and is also well shown in composite auricular grafts (q.v.). It was demonstrated by Staige Davis and Traut in 1925 that a true end-to-end anastomosis of capillaries occurs in 24 hours, and this precedes therefore by several days the ingrowth of capillary buds.

Infraclavicular and supraclavicular Wolfe grafts offer good quality skin from a potentially large area, but it may be necessary to repair the donor site by a secondary split skin graft.

Split Skin Grafts

Method of Cutting. Grafts of intermediate thickness, whether thin or thick, can be cut with a variety of instruments, the simplest of these being the Blair knife without any additional aids. It is the best instrument for cutting very thin grafts, but a good deal of skill and experience are necessary to cut wide and uniform grafts. An alternative instrument, well suited to the surgeon who only cuts grafts occasionally, is the Humby modification, where an adjustable roller lies immediately in front of the blade and assists in achieving uniformity. The best donor site is the thigh, preferably the inner aspect; the inner aspect of the arm gives skin of particularly fine texture, though the area is naturally smaller.

It is absolutely essential that the skin grafting knife, of whatever design, should be extremely sharp. A keen edge loses some of its quality in cutting even one graft. Unless

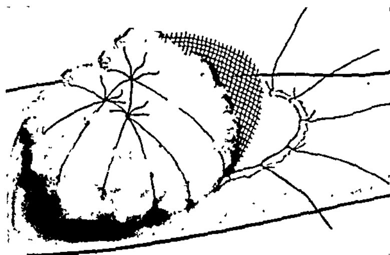


FIG 84. Diagram of split skin graft with appropriate dressings.

replaceable blades (of the razor type) are available, the knife must be stropped each time it is used.

The assistant holds the leg steady, with the thigh externally rotated and the knee slightly flexed so that the muscles are relaxed; at the same time, with his other hand held flat, he must push the thigh muscles towards the surgeon to present the maximum surface with the minimum curvature. The skin is kept taut and flat by a bevelled wooden board in the surgeon's left hand. This moves just ahead of the blade. The action of cutting must be smooth and uniform, the knife moving to and fro in a constant plane. All attempts to "press on" must be avoided.

The dermatome which was introduced by Padgett has had a wide vogue particularly in America, but is a difficult instrument to use infrequently. It does, however, offer two important advantages, since the graft can be cut to a constant three-quarter thickness, and the edges are of the same thickness as the rest of the graft. The dimensions of the graft are limited to 8 in. by 4 in. Other recent developments include pneumatically and electrically driven reciprocating dermatomes, but their use except by experts is not recommended.

After the graft is cut it must be protected in slightly moist gauze, as the effects of drying are damaging to the epithelial cells.

Method of Fixation. Split skin grafts may be fixed by a similar technique to that described for Wolfe grafts, particularly if they are of the thick variety. There are three aims in the proper fixation of all free grafts; normal tension, pressure, and immobilization. The graft in its new site should be under similar tension as compared with its original site; it should be subjected to a pressure not exceeding 30 mm. of mercury, or a quarter of the systolic blood pressure, using a crêpe bandage over cotton wool; and both the graft and the adjacent parts of the body should be sufficiently immobilized to prevent it being damaged by movement. It is usually best to place a single layer of tulle gras between the graft and the dressing to assist in separating these layers at the first dressing which is carried out at 5–7 days (Fig. 84). It is also possible, and on granulating surfaces advisable, to avoid extensive stitching; instead, the graft is spread raw side upwards on a sheet of tulle gras, and laid over the recipient area. It may be wise to suture the corners of the tulle gras to sound skin. In all cases great attention must be paid to hæmostasis. A layer of blood is an absolute bar to the entering capillaries, and many more grafts are lost from hæmatomata than from sepsis.

Management of Donor Area. Careless treatment of donor areas can lead to delayed healing and heavy scarring. The usual procedure is to cover them with damp swabs immediately after the graft is cut, and then at the conclusion of the operation, when hæmostasis is satisfactory, to replace the blood-soaked dressings with layers of tulle gras, gauze wrung out of saline, ample cotton wool and a bandage. A good alternative method involves the use of sheets of rayon next to the raw area. In either case the dressing should be left intact for 8 or 10 days, when it can be separated easily in an ordinary bath, and healing by that time should be complete.

Pinch Grafts

The indications for using this somewhat primitive type of graft are few. It should be reserved for cases where the "take" is doubtful, where it is difficult to cut a sheet of split skin thickness, and where the final appearance of the grafted area is unimportant. The grafts are cut by lifting a tiny area of skin with a straight needle, and cutting a circle 3 or 4 mm. in diameter with a No. 11 blade. These grafts are then conveyed on the point of the needle and placed on the raw area 1 cm. apart. Healing is slow and there is considerable scarring both of donor and recipient areas.

Epithelial Inlay Grafts

The application of skin grafts to raw areas other than on the surface of the body has been widely developed. Thin grafts can be maintained in accurate apposition to a raw cavity by a suitable mould of dental composition, and the skin will "take" in a very saisfactory way.

This technique has been applied successfully by McIndoe to two urogenital lesions, congenital absence of the vagina and hypospadias, and in the case of the vagina is undoubtedly the method of choice.

The method is also applicable to eye-sockets where there is a deficiency of conjunctival lining, and it is frequently used in the buccal sulcus to facilitate the wearing of an unusual prosthesis, or to increase the mobility of a cleft lip which is adherent to the alveolar ridge.

All epithelial inlays are very prone to contract rapidly during their first 6 months, and some appropriate mould or prosthesis must be worn for 24 hours a day to maintain the lined cavity. Fifteen minutes may suffice to produce a shrinkage which cannot be overcome.

Skin Banks

It is sometimes a great advantage, especially in the treatment of burns, to be able to store surplus skin. This enables the surgeon to have on hand extra skin which can be applied to secondary raw areas without an anæsthetic.

The skin is stretched and sutured to a sheet of rubber dam, or folded so that the raw surfaces are in mutual contact. It is then placed with sterile precautions in a suitable jar in such a way that it stands in a vertical plane. A gauze swab well soaked in saline is placed in the bottom of the jar, as it is essential that the air should be saturated with water vapour, but the graft must not be in direct contact with the saline itself. Skin is stored in an ordinary refrigerator at 2°C. and may be kept, under favourable conditions, for at least a month without prejudice to the eventual "take"; in many cases success has been achieved after much longer periods.

TRANSFERRED SKIN FLAPS

Direct Flaps

It is frequently necessary to transfer a skin flap directly from one site to another which is not adjacent. This single migration always requires at least two operative stages usually separated by an interval of 2–3 weeks. The first principal stage involves attachment of the skin flap to the defect, and during this phase there must be secure fixation of the two sites to prevent tension. The second stage involves detachment from the parent site, the remainder of the skin flap being sutured into its new position. In certain circumstances, but by no means as a matter of routine, a preliminary operation to "delay" the flap is carried out. This involves undermining all (or part) of the flap and suturing it back in its original position. This tends to enhance the blood supply when the flap is again raised 2 weeks later. It is apt, however, to cause some degree of œdema and subdermal fibrosis which is not helpful.

The outstanding example of a direct transfer is the cross-leg flap, and this may be explained in further detail as a general illustration of how all direct flaps are managed.

Cross-leg flaps must be designed with care and exactitude (Fig. 85). The best donor site is the calf of the normal leg. Before the flap is cut a preliminary experiment in design is essential, and this has been termed "reversed planning." The defect on the affected leg is defined and marked in ink; a "flap" of jaconet is then cut to fit this defect, with a sufficient "bridge" to reach the donor leg. Finally the pattern is transferred entirely to the donor leg, in reversed sequence of the operative plan, and in this way the flap is designed and marked on the donor leg. It is important that the length of the flap should not exceed its width (at its base) by more than 50 per cent. This maximum ratio of 1·5 to 1 applies to all body areas outside the face.

The exact cross-legged position is important to the patient's comfort and must be carefully studied. Most surgeons favour plaster of Paris fixation, and it is usual to put both legs in plaster the day before attachment, with a generous window on each side to give adequate access at operation.

The raw area both on the donor leg and on the under surface of the skin bridge or pedicle is covered with a split skin graft so that the entire procedure is a closed one. It is important to obtain as large an area of contact as possible when the flap is first sutured into its new position.

Once the flap has been attached close attention must be paid to its colour. Pallor, with a poor return of blood following gentle pressure, indicates an inadequate entry of



FIG. 85. Cross-leg flap during the phase of attachment showing plaster of Paris fixation. (Mr John Watson's case.)

arterial blood. Cyanosis is evidence of an unsatisfactory venous return. In practice most flaps with impaired circulation become cyanosed, at least in the later stages.

Direct abdominal flaps to the arm, wrist or hand are managed in a similar manner. "Delay" is seldom a necessary preliminary. The method is especially useful in patients with serious lesions of the deeper structures who will later need orthopædic or neurosurgical operations. A warning, however, may be given regarding the hazards of applying an immediate direct flap to a recent open injury. The danger arises not so much from the risks of potential sepsis, which are in fact negligible in most cases, as from the probability of thrombosis in the damaged vessels of the recipient area which may lead to delayed necrosis. An experienced surgeon may of course be able to assess this danger and may accept it as a "calculated risk." But the lessons taught by experience should serve as a warning, and it may be a wiser decision to treat the acute injury with a provisional free graft, and carry out a definitive repair with a skin flap as soon as healing is complete.

Indirect Flaps

Skin flaps can be carried from remote areas by the use of an intermediate host. The essential points are best illustrated by a single example. Let us suppose that the patient has a skin defect of the scalp, for which local skin is not available, and it is wished to bring up abdominal skin via the wrist. The surgeon designs the area of flap required on the abdomen, and then raises part of this skin flap along its lower edge; this can be set into a raw area which is established on the radial aspect of the wrist, by turning back a semicircular or rectangular flap; the latter will ultimately be returned to its original position,

and leave an inconspicuous scar. The wrist remains attached to the abdomen for approximately 21 days and, unless the abdominal flap is a very large one, it is then fully separated from the abdomen and brought up to the top of the head, where it is fixed for a further 21 days (Fig. 86). Such skin flaps are cut relatively thin, with only sufficient fat to protect the subdermal plexus of blood vessels. Excessive fat contributes nothing and is in fact parasitic in its demands on the limited blood supply.



(a) (b)

FIG 86 Sir Archibald McIndoe's case
(a) Attachment of transferred abdominal flap to wrist
(b) Secondary attachment of flap to scalp defect (electrical burn).

The essentials for success in these manœuvres are accurate planning and accurate fixation. It will be seen that there is a minimum of three operations, and the time in hospital is likely to be at least 7 weeks. Recent work suggests that this time can be safely shortened in expert hands, but the orthodox period of 3 weeks for each stage should not be lightly curtailed.

Indirect skin flaps are also useful in the repair of large skin defects of the lower leg, which for reasons of size or special difficulty are unsuited to cross-leg flaps. Again the wrist (or forearm) is used as a carrier or intermediate host, as in the example given. There are obvious difficulties in the somewhat acrobatic position necessary for final attachment of wrist to leg. These, however, are not so serious as might be imagined, and secure fixation is attained in most cases by Elastoplast strapping. Physiotherapy exercises are useful before and during attachment, as also in cross-leg flaps.

Tubed Pedicles

The principles governing the transfer of skin in the form of a tubed pedicle are similar to those already cited. Tubed pedicles, however, have the enormous advantage

that once they are raised there should be no risk of infection from any raw area, as the whole procedure is a closed one. However, certain very strict rules have to be observed.

The ratio of length to width should not exceed 3 to 1, and a useful size is 9 in. × 3 in. This gives a tube approximately 1 in. in diameter. If a greater length is required, the tube must accordingly be wider, but a short and broad tube is of course permissible.

The two best sites for raising a tubed pedicle are the flank or lower abdomen, and the thoraco-acromial area. It is sometimes possible to close the defect in the donor area by local flaps, but this involves tension, and therefore a free graft is often preferable. A number of technical points should be borne in mind. The full layer of fat should not be included, as it is apt to make the tube unduly tense. A tubed pedicle on the abdomen should be designed on a slight curve, to overcome the linear tension in relation to the convexity of the body. Suturing on the under surface should be accurate to avoid any possibility of sepsis, and particular attention should be paid to careful closure at the two ends. It should always be remembered that thrombosis, whether due to careless handling or inadequate protection, is likely to kill the pedicle.

Once it is safely established, a tubed pedicle can be moved, if necessary by intermediate stages, to almost any site on the body. The method of movement may be direct or indirect. Thoraco-acromial pedicles can be moved to the face or neck without an intermediate host, as the necessary approximation between shoulder and defect is usually possible. Fixation, however, must be sufficient to prevent tension, especially during the early phase of attachment.

Abdominal tubed pedicles can be moved by a series of local manœuvres, but in most cases indirect transfer is indicated and the wrist is used as a carrier. By this means most parts of the body, from vertex to ankle, can be reached. A curved or triangular flap is turned back on the radial aspect of the wrist, its size being designed to fit exactly the detached end of the tubed pedicle, once the latter's blood supply is established.

As a matter of routine it has been assumed by most surgeons that 21 days is the safe and proper period for each phase of migration. A simple calculation in any instance will show the total time that the complete series of manœuvres will take. For example a transfer from abdomen to neck will be planned as follows: First stage, elevation of pedicle; second stage, attachment to wrist; third stage, attachment between wrist and neck; fourth stage, secondary attachment to neck; fifth stage, pedicle is opened and spread. This occupies four intervals each of 3 weeks between the first and last operation, a total period of approximately 3 months.

In an effort to curtail this lengthy programme, a number of tests, simple and otherwise, have been described in recent years for testing the circulation at any stage of migration. Most of these involve some form of clamping of the established end, so that blood can only enter and return through the point of attachment which is in doubt. The systemic response to a local injection of atropine, or the detection of radio-active isotopes, are two of the many methods that have found favour.

It should be remembered that while tubed pedicles are capable of astonishing migrations, there may be unforeseen difficulties which can lead to serious trouble. There is no difficulty whatsoever in raising an impressive tubed pedicle, but to complete the necessary stages is sometimes risky, tedious, complex and disappointing, and the tests referred to above do not wholly remove the inherent hazards of the method.

SUMMARY OF ALTERNATIVE METHODS

It will be seen that the plastic surgeon has at his disposal a number of alternative methods for repairing skin defects, and some attempt must be made to set forth the factors which will influence his choice. In principle the order of preference will be:

(1) Local skin flaps.

(2) Free grafts.

(3) Transferred skin flaps.

With improving technique the scope of local flaps has steadily extended and they now have very wide applications. One obvious advantage of this method is the similarity in texture and colour of the flap in relation to the adjacent tissue. For instance, the skin of the cheek is sure to look better on the cheek than skin from elsewhere. A further advantage arises from the accessibility of local skin, and it saves much time if the operational field is confined to one area. Wherever necessary the secondary defect must be closed with a free graft, and in many cases this can be so arranged that this grafted area is either less important or less conspicuous than the primary defect. Local flaps are particularly applicable to areas where the blood supply would not sustain a free graft, or where there is a fistula or other compound lesion.

Free grafts, while generally inferior in appearance to local flaps, still have a very wide sphere of usefulness. They are particularly applicable to the initial treatment of acute injuries where the viability of the surrounding skin is in doubt, to recent burns where repair by flaps is impossible, and to defects following the excision of malignant disease, where a skin flap might conceal an early recurrence. Some special areas, notably the upper eyelids, are unsuited to any kind of flap, and should always be repaired with free grafts.

Indications for transferring skin flaps from a distance are numerous, especially in severe compound limb injuries. It is usually undesirable to cover exposed or damaged tendons or nerves with a free graft, and it may in fact be difficult to obtain a satisfactory "take," even with a temporary skin graft. However, in the case of the forearm and hand an immediate abdominal flap may be permissible. Where it is likely that orthopædic surgery will be necessary later, a repair by full thickness flaps must be undertaken either as a primary or a delayed procedure.

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Technique

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RECONSTRUCTION BY BONE AND OTHER TISSUES

BONE GRAFTING

Bone grafts play an important role in the field of plastic surgery. They are principally used in repairing defects of the frontal bones, the nose, the orbit and the mandible.

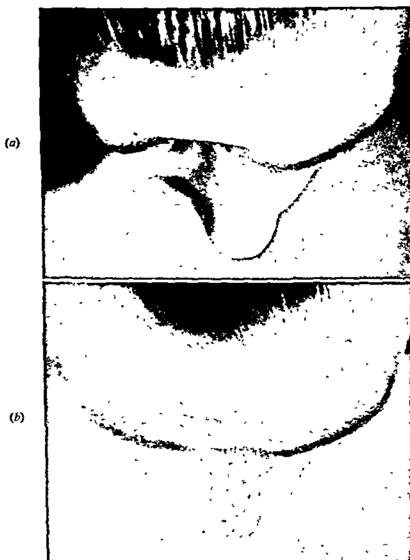


FIG 87 (*a*) Patient with contour defect following radical surgery for frontal sinusitis.
(*b*) Contour restoration by iliac bone graft

Frontal Area. Full thickness defects of the frontal bones are a problem usually for the neurosurgeon; but many patients have serious distortions of contour, not involving the inner table of the skull, in relation to the supra-orbital ridges and frontal sinuses. The majority of these involve no intra-cranial complications and are best treated by a bone graft. The bony defect should be defined and measured, and a plate of bone of the correct size cut from the ilium, just below the anterior part of the crest.

A good exposure is obtained if the iliacus muscle is reflected with the periosteum from the inner aspect of the ilium, and a plate of considerable size can be removed by chisel, leaving a negligible defect. The bone is trimmed and fitted to the frontal defect, with its cancellous surface outwards; this encourages an early entry of blood from the under surface of the overlying skin flap. Fixation by wire is often unnecessary if the bony carpentry is accurate. In some cases additional bone chips may enhance the contour (Fig. 87).

Nose. Many patients with deformities of the nasal bones require refracture and trimming of the bone rather than a graft. However, nasal defects with loss of bony contour, and certain deformities involving the tip of the nose, are best treated by a simple bone graft. This is designed as a so-called "cantilever" graft, and has a wedge-shaped outline in profile (Fig. 88). It is taken from the iliac crest, and is trimmed so that only a dorsal strip of cortical bone is left, the remainder being cancellous. The columella and septum are split and a subcutaneous tunnel prepared over the bridge of the nose almost as far as the glabella. The upper portion of the tunnel is small enough to hold the top end of the graft securely without any further fixation. Bony union is encouraged by stripping the adjacent nasal periosteum, but it is impossible to establish a sub-periosteal tunnel. About 50 per cent of patients develop bony union, but this is by no means essential to success.

This technique is so satisfactory that more complicated methods, such as the hinged or L-shaped graft which obtains support from the nasal spine, are seldom indicated.

Orbit. In the treatment of bony lesions of the orbit bone grafts have been attempted for two purposes—to improve the contour of an unreduced fracture of the malar or frontal bone, and to relieve an associated diplopia.

For reasons given in a later section, the best treatment for unreduced malar fractures is refracture, mobilization and fixation in the correct position. If this proves impossible, camouflage may be necessary and a bone graft may be useful. The use of bone to correct a downward displacement of the eye is not always successful in curing a positional diplopia; however, this serious disability must be alleviated, and either cartilage or some other substance may be placed more easily than bone in the precise position necessary to give the proper elevation.

Mandible. The principal indications for using a bone graft in relation to the mandible are three: to fill a bony gap whether due to surgery, trauma or disease; to establish bony union in cases of non-union or delayed union; and to correct or conceal a faulty contour.

Certain criteria are essential if these procedures are to prove uniformly successful, as they should do. A wide exposure is necessary, and the incision must be so placed (usually an inch below the lower border of the mandible) that the mandibular branch of the facial nerve is preserved. The bony defect is defined, and the correct gap (if any) *established*. The buccal mucosa must not be wounded, or, if an excision of bone with attached mucosa has just been carried out, it must be carefully repaired. A bony shim from the ilium is cut consisting mainly or wholly of cancellous bone. Accurate apposition and fixation is achieved by wires through precisely placed drill holes. Cancellous bone chips may be used to encourage new bone formation. Immobilization of the mandible is required and is the responsibility of an expert dental surgeon. Direct inter-maxillary fixation, by uniting upper and lower dental cap splints already cemented in position, *may suffice. Occasionally* external splinting, with pinning of the posterior fragment, is required.

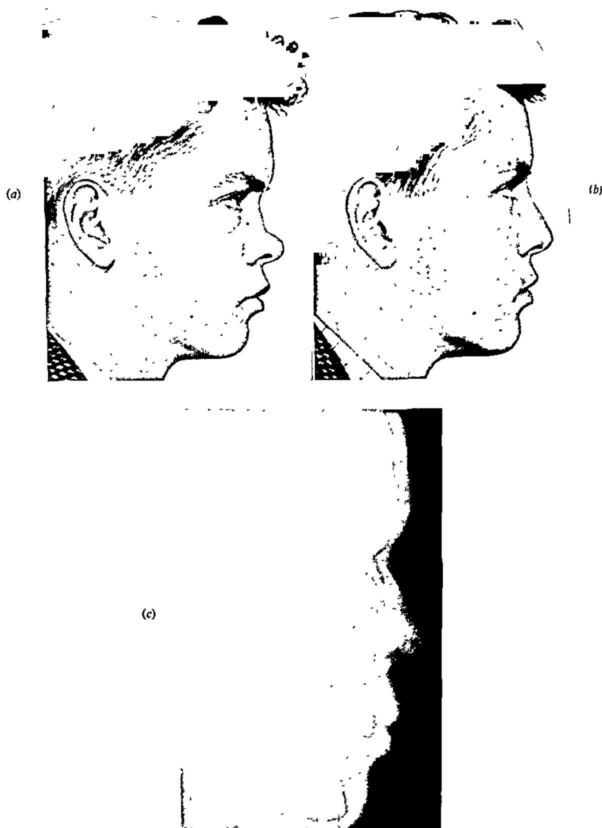


FIG 88. (*a*) Saddle deformity of nose due to septal abscess.
(*b*) Patient after bone graft
(*c*) X-ray of bone graft 6 months later.

REPAIR BY OTHER TISSUES

Cartilage Grafts

The applications of cartilage grafts have been intensively explored during the past 10 years. The main objection in earlier years to their extensive use was related to the difficulties and discomforts in obtaining sufficient tissue from the costal cartilages of the patient himself. Recently the use of human homografts and animal heterografts has been developed and cartilage "banks" have been established. The varieties available are briefly as follows:

(1) Cadaveric cartilage. These homografts are taken from suitable post-mortem cadavera, the appropriate costal material being removed en bloc. They are then cleaned and prepared under sterile conditions and placed in 1 in 100 aqueous merthiolate solution. After appropriate tests of sterility they are finally transferred to a 1 in 8,000 solution and stored in a refrigerator at 2°C.

(2) Bovine cartilage. This may be prepared under similar conditions from fresh slaughter-house material, or it may be obtained already prepared and sterile from a commercial manufacturer.

(3) Whale cartilage. This material which is remarkable for its bulk and homogeneity is under trial. Its preparation is similar to human cadaveric cartilage.

The choice between these different sources at present depends on the bulk required, the material available, and on personal experience and preference. Cartilage grafts may be used in one of two states: as a solid sheet or peg, like a bone graft; or in the form of small slices or tiny cubes, which are known as "diced" cartilage.

The indications for cartilage grafting are therefore of two kinds: it may be used as an alternative to bone in the conditions already outlined in that connection. The advantage of using preserved cartilage as opposed to autogenous bone is obvious, as it imposes much less discomfort on the patient. But it has been clearly shown in recent researches that cartilage undergoes slow but progressive absorption and may also suffer distortion. These disadvantages are not absolute, but should be weighed in every case before a decision is reached. A special warning is necessary regarding the risks of secondary distortion with nasal grafts.

The second group of indications for cartilage grafting concerns the use of diced cartilage. This form of cartilage is useful to fill an abnormal depression or to produce a minor modification in contour. It is best used where the defect is clearly defined so that the diced fragments are readily maintained in the correct position, and where the disturbing factors of tension or pressure are largely absent.

A special application of diced cartilage is in reconstruction of the external ear. (*See* page 266.)

Mucosal Grafts

The transplantation of mucosa would have a wide sphere of use if it were simple or practicable to find suitable donor sites. In fact the lining of the cheeks is the only satisfactory donor area, and the amount of tissue available is small. For this reason most mucosal defects require an epithelial inlay graft (q.v.). The main indication for a mucosal graft is to enlarge an eye socket which is of inadequate size to hold a prosthesis. A skin graft in a socket has the serious objection of tending to smell, and adequate hygiene is not easily achieved by the patient.

Mucosa is useful especially when only a partial reconstruction of the socket is required, as it can be used in conjunction with such normal conjunctiva as remains; in these circumstances skin is not suitable.

Fat, Dermal and Fascial Grafts

Grafts of fat, either alone or attached to the adjacent dermis, are used as material for "plumping," that is, to fill contour deficiencies. Grafts of fat alone undergo considerable shrinkage with at least a 50 per cent decrease in bulk due to progressive fibrosis.

Some surgeons prefer to take the fat together with its overlying skin from which the epidermis has been removed, as in skin grafting. This gives a more manageable sheet of tissue and slightly modifies the effects of fibrosis. It is especially appropriate to contour defects of the eyelids caused by loss of peri-orbital fat. The inguinal region is a useful donor area.

Fascial grafts are seldom used in plastic surgery except in the form of strips from the ilio-tibial tract. Fascia in this form plays an important part in the relief of permanent facial paralysis, and this condition is of sufficient importance and difficulty to be considered here at some length.

Facial Paralysis

The problem of permanent facial paralysis is both serious and complex. Its various aspects have been explored by neurologists, otologists, and general surgeons; but the plastic surgeon is only concerned with one aspect. His task is to provide static and dynamic support for those patients with permanent and irrecoverable lesions of the facial nerve, who (for whatever reasons) are unsuited to neurosurgery.

It is very important that patients should be properly selected before they are submitted to such operations. Unquestionably, reconstitution of the facial nerve, whether by suture, graft or decompression, is the best treatment where it is possible. There are, however, many cases in which nerve repair is likely to be hopeless; for instance, after radical removal of a malignant parotid gland, in certain middle-fossa fractures, in congenital lesions, in birth injuries, or in long-standing palsies In quite a different type of case, where there is very slow recovery, it may be wise to give temporary support.

With each patient the defect must be analysed carefully. In a fully developed paralysis there will be sagging of the mouth and of the cheek, ectropion of the lower lid, and lowering of the eyebrow on the affected side The patient himself may complain of dribbling, of difficulty in chewing, or of asymmetry of his mouth with an appearance of depression and stupidity; also of epiphora and lagophthalmos. Corneal ulceration is rare.

A great variety of material has been used by different surgeons to support the face, but fascia lata is undoubtedly the best. It is strong and not prone to stretch. It should be taken, preferably by open operation, from the toughest portion of the fascia lata—namely the ilio-tibial tract. This is in fact the tendon of the tensor fasciæ latæ, and is covered with paratenon. For clinical purposes it may be regarded as a flattened tendon and it retains all the characteristic advantages of a tendon even under tension. When transplanted it behaves as a living graft nourished by small ingrowing blood-vessels.

To obtain reactivation one must use muscle. Strips of muscle, partly torn from their parent muscle belly, are not ideal. They are likely to become separated from their nerve-supply and blood-supply, and they will then undergo fibrosis and cease to act as muscles.

But the use of a complete muscle, with its tendon intact, in conjunction with fascia lata is a very satisfactory combination.

Technique of Static Support. In static support there must be two fixed points. The lower point lies at the corner of the mouth, though it is also linked medially with the functioning half of the oral sphincter on the unaffected side. The upper point of fixation is usually the temporal fascia.

The operation is carried out as follows:

Three tiny incisions are made, one on the upper lip, one on the lower, and one on the lateral side of the mouth on the paralysed side. Two strips of fascia lata ¼ in. wide have



(*a*) (*b*)

FIG 89. (*a*) Patient with complete right-sided facial paralysis of 10 years' standing following removal of malignant parotid gland.
(*b*) Patient 10 months after temporalis transplant.

already been cut, one 7 in. and the other 5 in. long. The longer of these is then inserted with the Blair fascia needle in a figure-of-eight so that it reaches the unparalysed portion of the sphincter just beyond the midline in both upper and lower lips. The two ends are brought out of the lateral incision and sutured together with silk. The second strip is looped round the double loop at the corner of the mouth. It is then brought by means of a fascia needle deep to the skin, masseter and zygomatic arch, and brought out through a small incision immediately above the zygoma. Here it is securely sutured under proper tension to the temporal fascia.

Considerable "overcorrection" has to be produced, because the muscles on the unparalysed side are without tone under the anæsthetic. It is also important to adjust the tension of the figure-of-eight so that the mouth is not made too small.

A well-judged static operation will tend to straighten the nose, and centre the philtrum; it will control any bulging of the buccinator muscle, and it should also restore the normal curve of the cheek.

Reanimation by Dynamic Support. Muscle transplantation cannot hope to give the quality of reanimation that nerve surgery can achieve; but where the latter is not feasible, it offers the best alternative. It is the method of choice where there is an irrecoverable nerve lesion, where the patient is over 12 but under 50 years of age, and where

he is co-operative and intelligent enough to make the best use of an unusual and anomalous means of expression (Fig. 89).

The best method is to use the temporalis in its entirety, firmly secured to a strip of fascia lata (Fig. 90). It involves a direct open approach to the coronoid process of the

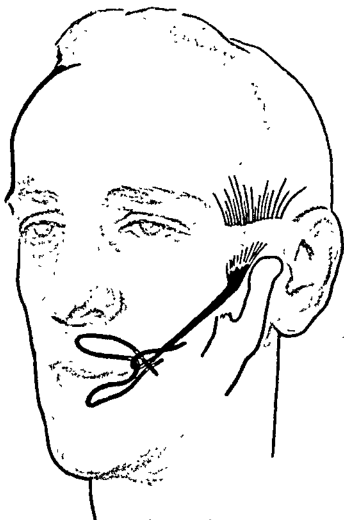


FIG 90 Diagram to indicate disposition of the two fascial slings in relation to transplantation of the temporalis.

mandible, so that the whole insertion of the temporalis muscle may be detached. There are several possible routes to the coronoid, which is surprisingly inaccessible; the best approach appears to be as follows:

An incision is made just above the lower margin of the zygoma, through skin and the superficial layer of the temporal fascia, down to bone. This fascia, which also constitutes the main origin of the masseter, is peeled off the zygoma sub-periosteally and the deep fibres of the masseter are then divided. Immediately below lies the temporalis tendon with its insertion into the coronoid. The latter is divided, removing 6 or 10 mm. of bone. This bone carries the temporal muscle insertion, and in this way the entire muscle is available for transplantation. The manœuvre is completed by suturing the second strip of fascia lata securely to the tendon, and making a small subcutaneous tunnel

to the corner of the mouth where the fascia is fixed to the figure-of-eight. The masseter is then firmly reattached at its origin.

In the early post-operative phase it is important to encourage gentle, active movements within the limits of comfort, for adhesions are the most likely complication with this type of operation.

Paralytic Ectropion. Ectropion of the lower eyelid is best relieved by an over-lapping lateral tarsorrhaphy using the writer's method (Fig. 91). This will carry the tarsal plate both up and out, and will restore not only its proper position but its normal tension. At the same operation as the tarsorrhaphy, it is also necessary to enlarge the lacrimal punctum. This is done by what is known as the "three-snip" operation. This makes a new ostium much nearer the sac. If these methods are properly carried out, the tears will drain into the nose quickly enough for the eye to remain dry under normal conditions. The eye will be sufficiently covered when the lids are open, and the cornea will be safe when the patient is asleep.

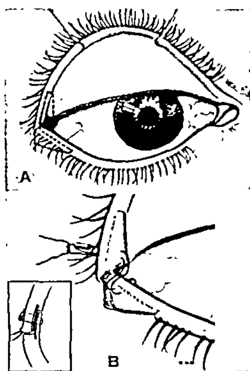


FIG. 91 Diagram showing.
(*a*) The incisions
(*b*) *The method of suture for a lateral tarsorrhaphy* with overlapping of tarsal plates

Some degree of epiphora is present in most of these patients and it should never go untreated, since the overflow of tears can be greatly reduced —*if not cured—by these very simple methods.*

Bilateral Paralysis. Paralysis of both sides of the face is usually a congenital condition due to agenesis of the nucleus of the seventh cranial nerve on both sides; it is frequently associated with some degree of oculomotor paralysis. The general effect on the patient's appearance and morale is deplorable, and any measure of relief is worth consideration.

Since drooping and immobility of the lower lip is an outstanding part of the defect, attention has been directed towards this part of the disability. Rigid support is not satisfactory, as not only will the face remain totally devoid of expression, but it is then difficult for the patient to open his mouth. Two fascial slings are accordingly inserted at the mid point of the lower lip, and brought up, one on each side through the tissues of the cheek, deep to the zygoma. The temporalis is exposed at the upper margin of the zygoma and the fascial strip fixed to the muscle in continuity. Suitable tension and support are achieved by then uniting the two strips in the midline of the lower lip. A secondary attachment is provided between sling and modiolus at the corner of the mouth, and this enhances a small degree of animation.

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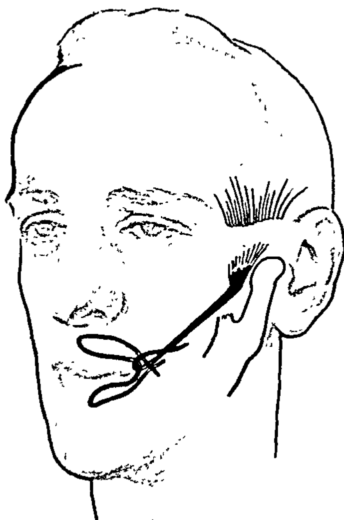


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Classification. The most satisfactory classification is that introduced by Ritchie. He designated the alveolus as the determining anatomical landmark, and established by this means three groups of cleft.

Group 1. Pre-alveolar clefts: These involve only the tissues anterior to the alveolus, constituting simple cleft lip.

Group 2. Post-alveolar clefts: These involve tissues posterior to the alveolus, namely the hard and soft palate; these comprise all those cases of cleft palate in which the lip is intact.

Group 3. Alveolar (or complete) clefts: All tissues are involved in these cases, from the margin of the lip to the uvula (Fig. 92).

This classification does not deal satisfactorily with certain rare cases where there is a cleft of the lip and alveolus but not of the palate. Patients with independent clefts involving the margin of the lip and the soft palate are included under both Group 1 and Group 2.

Incidence. There are a number of remarkable findings, common to all investigators, concerning the statistics of cleft lip and palate. It is found that the ratio of left to right sided clefts is about 2 to 1, as is also the ratio of male to female clefts in general. However, in Group 2 there is a definite female preponderance. No reasonable explanation has been put forward to account for these surprising facts. Approximately 25 per cent of all cases are bilateral. The over-all incidence of cleft lip and palate in relation to live births has been variously stated; estimates vary from 1 in 600 to 1 in 1,700. It is safe to assume that 1 in 1,000 represents a likely average. In terms of Ritchie's classification the relative frequency of the 3 main groups of unilateral clefts is roughly as follows: Group 1, 25 per cent; Group 2, 25 per cent; Group 3, 50 per cent. These figures, though only approximate, show little deviation from more detailed statistics.

Embryology

The reader will be familiar with the classical picture, contributed by His and other nineteenth century embryologists, of the early development of the face. Since 1910 a good deal of doubt has been thrown on their assumption that clefts between the maxillary and fronto-nasal processes are present at an early stage of fœtal life, but in normal circumstances disappear owing to coalescence and fusion. It is now suggested that the alleged clefts between various processes are in fact grooves which do not communicate with the naso-oral cavity, and that these grooves are only temporary. Veau was one of those who questioned the accepted ideas of coalescence. His view, briefly, was as follows: cleft lip may be due to a failure of the mesoderm from one side to penetrate the central part of the lip. Such failure would lead to one of two results: either there would be a complete rupture of the epithelial membrane, and this would cause a fully developed cleft lip; or there would be a partial rupture, with the formation of a narrow bridge of skin or an occult cleft with a gap in the muscle, the skin being intact. Each of these conditions is commonly found.

As regards isolated cleft palate it is clear that the palatal processes have failed to fuse at any stage, though the exact embryology is still debated. It must be remembered that clefts which are first observed at birth have in fact been present from an early stage in fœtal life, and secondary changes occur during the last 6 months of intra-uterine life which further modify the deformity.

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CLEFTS OF LIP AND PALATE

Introduction. Although exact statistics are not available, it appears probable that between 500 and 800 children are born in Britain every year with a cleft involving lip or

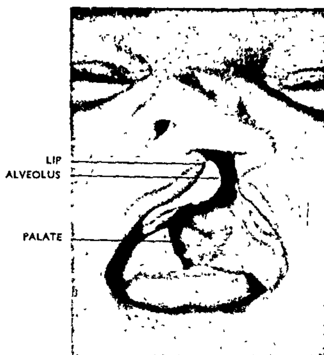


FIG 92 Complete cleft showing defect involving three elements—lip, alveolus, and palate

palate. The problem which these deformed children pose is a serious one, with economic, domestic, and surgical implications.

Although cleft lip and cleft palate are frequently associated, it is important that they should be distinguished not only in treatment, but with reference to embryology, ætiology, and incidence. It is now time that the misleading term "harelip" should be abolished, as it has not even the merit of being descriptively accurate.

The different types of cleft include varying degrees of simple cleft lip and simple cleft palate, as well as clefts that involve both lip and palate. Clefts may occur on either side or be bilateral. Central or median clefts are extremely rare.

be treated with due respect, they must not be interpreted in a rigid or unimaginative manner.

The child should be at least 10 lb. in weight, and gaining weight; he should not be less than 2 months old and if older should have reached his expected weight; and his hæmoglobin level should be not less than 11·8 gm. per cent (i.e. 80 per cent by the Haldane method), in so far as this is possible. Careful feeding with regular oral iron is usually sufficient; but occasionally a debilitated child may need intra-muscular iron, or even a blood transfusion. It is preferable to transfuse the child at operation, rather than as a preliminary measure.

Analysis of Defect. A child with a fully developed cleft lip suffers from a complex deformity, even when the palate is intact.

There is a complete gap in the muscles forming the oral sphincter, and this gap is increased by the unopposed pull of the muscles in each lateral element. The configuration of the red margin is altered and there may be a shortage both in the vertical and the horizontal axis. Frequently there is an occult cleft of the alveolar ridge, partly concealed by a muco-periosteal bridge. In such cases, as in all complete Group 3 cases, there is a tendency for the pre-maxilla to rotate forwards, hinging on the "normal" side.

Finally there is distortion of the nasal tip which deviates away from the cleft, with obliquity of the columella, flattening of the affected nostril, and deformity of the alar cartilage.

Surgical Aims. On account of these compound and inter-related deformities, the problem of repair must be considered anatomically in terms of nose, alveolus, mucosa, and muscle, as well as of skin.

The integrity of the sphincter must be restored, the line of the red mucosal margin reformed without distortion, the functional mobility and normal eversion of the lip established, and the nasal deformities corrected. Ideally, a single inconscipuous scar should be the only legacy from these procedures, which may however involve two or three operations during a period of 15 years. All this requires careful planning based on a sound surgical policy.

Repair of Lip

Pre-operative Care. The child, who should have reached the standards already described, is admitted to hospital a few days before operation. He should be trained to spoon feeding. A general assessment of his fitness for surgery, made by an experienced Sister, is of great value; an unfavourable verdict should be accepted even in face of satisfactory blood tests, etc.

An early morning feed is given as usual, and if possible the operation should be timed to come at the start of the morning's list. Premedication should be sufficient to allow the child to reach the anæsthetist asleep. Endotracheal anæsthesia is essential and the pharynx must be carefully packed. The child lies on a pillow with the neck slightly extended (Fig. 93).

Technique in Unilateral Clefts. The simplest design for repair may be the best choice for the less experienced operator; in principle this involves a narrow marginal paring of the edges of the cleft to establish an inverted V-shaped defect. This method was developed with great success by Victor Veau of Paris and described in detail in his book, "Bec-de-Lièvre."

Ætiology

The ætiology of cleft lip and palate is still a matter of considerable controversy. It is, however, clear that there are two possible factors: (1) genetic, and (2) environmental. As regards the latter, alterations in the environment during intra-uterine life are of two kinds: (*a*) systemic, and (*b*) local or mechanical.

Genetic Factors. Very careful case records, particularly by Fogh-Anderson, suggest that approximately 30 per cent of all cases have some familial history of a similar defect. This fact establishes beyond all doubt that heredity is an important factor. The following findings are also of some genetic interest: where one parent is affected, the first child will have a cleft lip or palate in only 2 per cent of cases, but this may rise to 15 per cent in families where one parent and at least one older child is involved. As the incidence with normal parents is approximately 0·1 per cent, the significance is obvious.

Isolated cleft palate (Group 2) does not conform in incidence or ætiology to the same pattern as Groups 1 and 3.

It is believed that neither simple dominance nor recessivity can explain the known facts, but it is possible that the effects of abnormal genes may be conditioned by the general genetic pattern of the family or individual in question, and thus complicate the findings in any statistical survey.

Environmental Factors. Attempts have been made to prove that maternal malnutrition or disease in early pregnancy is an ætiological factor. There is, however, no incontrovertible evidence to support this view, and neither poverty nor rubella can be held responsible. It need hardly be stated that the popular lay view of sudden emotional disturbances being a likely cause is quite without foundation.

A number of unusual circumstances, such as a child born with a finger or an amniotic band in the cleft, have led to an undue emphasis on a local factor. This explanation, however, appears very unlikely if only for the reason that these cases constitute rare exceptions, and in general there are no such mechanical obstructions to be seen.

Associated Deformities. Children with cleft lip and palate unfortunately show a considerable predisposition towards severe physical and mental defects, amounting to not less than 10 per cent. The more severe deformities such as hydrocephalus are usually fatal, but conditions like spina bifida and talipes are by no means rare; there is also a relatively high incidence of mental deficiency.

CLEFT LIP

Infants with simple cleft lip have a double disability—functional and cosmetic. The functional defect, when it affects the baby's capacity to suck, is highly important; but it is the horrifying appearance of the child which is apt to weigh most heavily with the parents, and make them press for an early operation. If there is also a cleft palate the feeding difficulties may be considerable; but unless the child is premature, spoon feeding can be taught, and proper nutrition achieved. In many cases, a bottle with a large teat gives good results, and in not a few the ideal of breast feeding is possible. The capacity to suck may in fact be normal.

Criteria of Operation. Experience has led surgeons and anæsthetists to establish certain standards before submitting babies to a major procedure. While these rules should

be treated with due respect, they must not be interpreted in a rigid or unimaginative manner.

The child should be at least 10 lb. in weight, and gaining weight; he should not be less than 2 months old and if older should have reached his expected weight; and his hæmoglobin level should be not less than 11·8 gm. per cent (i.e. 80 per cent by the Haldane method), in so far as this is possible. Careful feeding with regular oral iron is usually sufficient; but occasionally a debilitated child may need intra-muscular iron, or even a blood transfusion. It is preferable to transfuse the child at operation, rather than as a preliminary measure.

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The practice of marking the lines of incision in ink at the start of the operation is wise, and it is helpful if the exact points on the red margin which must be finally approximated are "tattooed" by pushing a nib or needle carrying ink through the skin.

In all standard procedures the mucosa, muscle, and skin are freely mobilized, particularly on the side of the cleft. Incisions are made in the mucosa on each side along its line of reflection from the alveolus. The dissection on the cleft side is carried upwards and outwards from the alar base. Wider undermining extending over the nose and up to the orbit is not recommended as a routine, especially if it causes needless damage to the periosteum of the maxilla. The cut edges of the oral sphincter are carefully defined, and the marginal skin of the cleft is undermined, but only to a small and necessary extent.

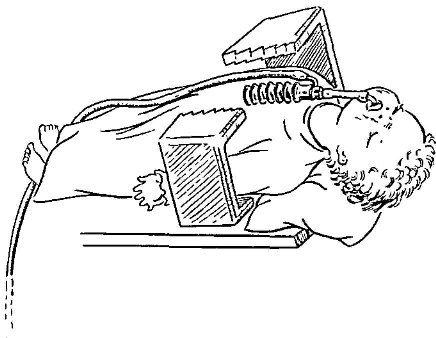


FIG. 93 Position of baby on table (note bridge for protection of child's chest)
(From "Cleft Lip and Palate" W. G. Holdsworth, Heinemann)

The three layers are repaired independently, beginning with the mucosa of the buccal fornix; then the muscle is sutured starting at the nasal floor and working downwards; finally the skin and remaining mucosa are closed. Tiny stitches of the finest silk or gossamer silkworm gut are used for the skin, and plain catgut for the mucosa and muscle.

Careful reconstitution of the floor of the nostril, and extreme accuracy of apposition at the red margin are two points of particular importance. It is useful to carry a small flap of mucosa towards the midline just below the red margin and thus avoid an entirely vertical scar.

The best results of Veau's method are excellent, but children who form heavy scars are likely to suffer a slight though ugly notching of the red margin. This deformity is also sure to develop if there is the slightest breakdown of the suture line at the junction of skin and mucosa.

Le Mesurier Operation. In the hope of avoiding the tight notched lip that is not

uncommon after repair, Le Mesurier of Toronto published in 1948 a new procedure, based in principle on Hagedorn's work of 60 years ago. It is designed to give a loose lip with a natural outward roll of the lower edge, and it avoids a straight vertical scar. The

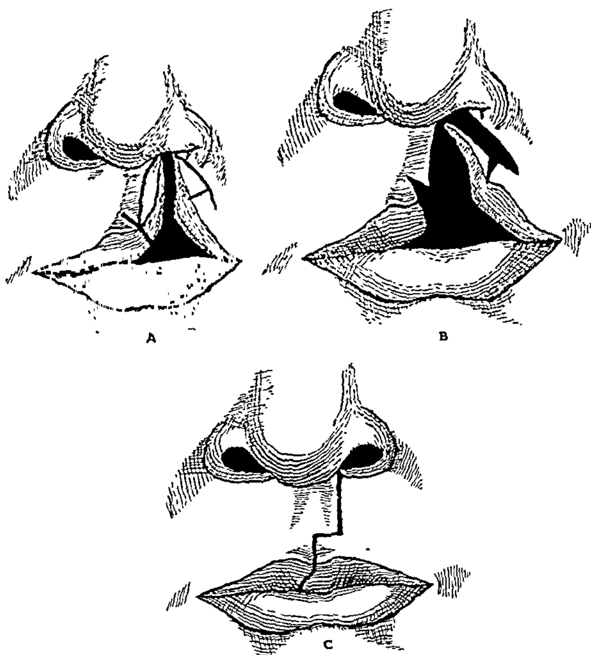
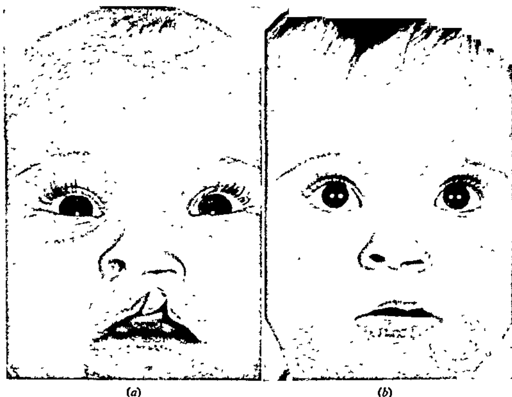


FIG. 94 Le Mesurier operation Diagrams showing (*a*) the incisions, (*b*) the right-angled flap, and (*c*) the final scar

final scar consists of one horizontal and two vertical components, due to the introduction of a tiny right-angled flap. The details of the incision and the repair are shown in the diagrams (Fig 94). This is not a simple procedure, but the results obtained by experienced surgeons who have given it an extended trial are proof of its essential merits, and it constitutes an important advance (Fig. 95).

Post-operative Management. The child is so anæsthetized as to regain consciousness quickly. It should be given a feed as soon as it is fully co-operative. Whether or not a Logan bow is used to avoid tension at the suture line, the child must be restrained from touching the wound. Light cardboard or plastic splints are applied to the arms to prevent flexion at the elbow, and in certain instances it will be further necessary to secure the splints to the sides of the cot. It is important to prevent scabbing of the suture line, and the application of a little grease is helpful. Any scabs that do form should be gently



(*a*) (*b*)

Fig. 95 (*a*) Cleft involving lip and alveolus with moderate nasal deformity.
(*b*) Patient 6 months after operation.

(This is an average, not an exceptional, result by the Le Mesurier method.)

removed by moist gauze. The removal of stitches should be carried out with discrimination according to the exact condition of the suture line, and a rigid routine should be avoided. It is usually possible for the last of the stitches to be out at the end of 5 days; but the consequences of removing stitches too early are serious.

Repair of Anterior Palate

In Group 3 cases, repair of the nostril floor should be undertaken at the same time as the primary surgery of the lip. If it is left for a year until the main operation on the palate is undertaken, access is greatly reduced by the presence of the repaired lip. It is the practice of many surgeons to include the nasal mucosa of the entire hard palate in this repair, but the need for this extensive early reconstruction is a matter of opinion.

At one time it was believed that this anterior closure must be carried out in two layers, the nasal mucosa being reinforced by palatal muco-periosteum. But the palatal flap

described by Veau in his classic treatise "Division Palatine" fails to reach the important area just posterior to the alveolus, and it therefore appears to be of doubtful advantage. The usual modern procedure consists of an exacting and thorough separation of mucosa from alveolar margins, septum and lateral nasal wall. The two mucosal flaps thus formed are turned in towards each other and united by mattress sutures. This is often a difficult manœuvre particularly in a narrow cleft; but it is well worth the trouble especially in terms of the later closure of the palate.

Bilateral Clefts

Bilateral clefts of the lip, and in particular the large group where the palate also is cleft, constitute a formidable problem in repair. In addition to a mere doubling of the unilateral lesion there is anterior displacement of the premaxilla and a shortage of muscle and mucosa in the prolabium. This apparent excess of bone and lack of muscle greatly increase the difficulties of closure (Fig. 96). There are also serious feeding difficulties, while the baby's alarming appearance causes great distress to the parents.



FIG. 96. Baby with bilateral cleft lip and palate, showing characteristic prominence of premaxilla.

In addition to the principles of repair mentioned in relation to unilateral clefts, the surgeon must take into consideration the special anatomical difficulties and draw up a plan of procedure accordingly.

In bilateral clefts involving lip alone, the premaxilla is in its correct position and closure may be undertaken at 3 months, with simultaneous repair of both sides. Where the palate and alveolus also are cleft, it may be possible to repair the lip and nasal floor on both sides at one operation, if the premaxilla is lying fairly favourably. In these cases the remarkable moulding influence of the repaired lip assists in a satisfactory alveolar arch. In unfavourable cases, with marked anterior displacement of the premaxilla, a different plan is indicated. Some surgeons of great experience have advocated the preliminary repositioning of the premaxilla, removing the necessary bone from the anterior portion of the supporting septum (known as the pre-vomer), and fixing the mobile premaxilla by metal pins. This method, in so far as it disturbs the blood supply, carries a risk of atrophy and cannot be advocated as a standard method. It is, however, essential that the premaxilla which is the keystone of the alveolar arch should not only be preserved but caused to lie in its correct position.

In the most difficult cases the best compromise may be as follows: the soft tissues of the lip are repaired on one side to guarantee the blood supply to the premaxilla: a few weeks later the latter is set back into position with resection of the pre-vomer and at the same session the second side of the lip is repaired. The lip then acts as a sufficient splint, and there is little or no risk of bony absorption due to ischæmia.

There are many views on the best design for repairing the soft tissues in bilateral clefts. Whatever method is favoured, it must be remembered that there is no muscle in the prolabium, and the surgeon should therefore aim at uniting the separated muscle elements directly to each other; the prolabium will then lie not between but in front of the reconstituted sphincter.

It is often unnecessary to retain the red margin of the prolabium, as the mucosa from each side should be united in the midline if this is possible without tension. Sometimes the prolabial skin appears excessive, and it is tempting to push it up into the base of the columella; but this is seldom satisfactory.

In general, early surgery should be planned so as to cause the least damage and disturbance to growth, while orthodontic supervision should be sought without delay to prevent, as well as to cure, alveolar deformities.

Secondary Deformities of Lip and Nose

It is not always possible at the primary operation fully to correct the complex deformities associated with severe clefts of the lip. In these circumstances patients are liable to show the following secondary features: the tip of the nose is deviated away from the cleft; the alar cartilage on the affected side is flat and kinked and its apex lies too low; the nostril floor is too wide; and there may be distortion of the red margin of the lip due to the pull of a vertical scar. In addition small errors at the primary operation may result in a gap in the oral sphincter or irregularity of the mucosa. The adequate correction of these faults usually entails "taking the lip to pieces," and carrying out a radical correction of the septum and alar cartilage, as well as a meticulous trimming and resuture of the lip in three layers.

For patients where the height of the red margin is not equal on the two sides, or where the lip looks too long in relation to the visible area of mucosa, Gillies has described a most useful procedure, which he calls the Cupid's bow operation. This involves establishing a new mucosal line by an extact and minimal excision of skin. The mucosa of the lip is mobilized and, after advancement in a vertical direction, is sutured to the corrected margin of the lip. This effectively restores symmetry and balance in certain difficult cases.

In bilateral clefts the secondary difficulties are even more troublesome and awkward to resolve. The critical problems are as follows: the pre-maxilla may be stunted and the four incisor teeth which it should carry may fail to erupt; (the lateral incisor is frequently absent in relation to any alveolar cleft). The columella is short and this depresses the tip of the nose. There may be a gross shortage of skin in the prolabial area. The general effect on the patient's appearance, especially in profile, is disastrous.

The relief of these complications is planned briefly on the following principles. The correct alignment on the alveolus is reproduced by a dental prosthesis with such teeth as are missing. The tight lip may require new tissue, either from an epithelial inlay if there is a shortage of mucosa, or by a full thickness pedicled flap from the lower lip. This useful but tricky manœuvre, the Abbe operation (Fig. 97), is carried out in two stages, and involves the lips being partly sealed for 18 or 21 days. Finally, the columella may require lengthening to release the nasal tip. This can be achieved by a variety of methods; the choice includes a V-Y advancement (one of its rare applications), a free auricular graft, or the use of local flaps.

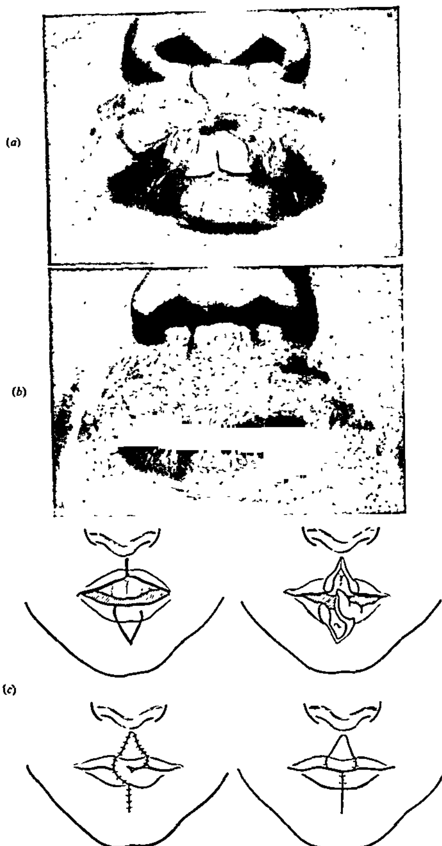


FIG 97. Mr. F. T. Moore's case.

(a) Adult patient with very severe scarring of lip in relation to bilateral cleft.
(b) Appearance after Abbe operation (prior to excision of outlying scars).
(c) Diagram indicating technique of Abbe operation

CLEFT PALATE

The principal disability arising from clefts of the palate is a disturbance of normal speech. For this reason the functional consequences of cleft lip and cleft palate are entirely different. Normal speech depends, amongst other anatomical factors, on a capacity to exclude the nasal from the oral cavity. Integrity of the roof of the mouth is not enough; there must be an airtight closure of the naso-pharyngeal sphincter. This sphincter, which is formed by the palatal muscles acting in conjunction with the superior constrictor of the pharynx, brings the upper surface of the soft palate into contact with the posterior pharyngeal wall. Two points should be noted: the posterior free edge of the soft palate is not the essential point of contact; and the pharyngeal wall is not passive, but moves in an anterior direction towards the palate; this action produces the muscular prominence known as Passavant's ridge, though the point of palatal contact tends to be just above this ridge.

Analysis of Defect. In a cleft involving the whole length of the palate the defect may be considered in two parts. The anterior deficiency of the hard palate constitutes a static defect; there is a gap involving three fixed layers—the bony palatal process with its nasal and oral mucosal coverings. The posterior deficiency of the soft palate is not a static defect; there is an inconstant gap between two mobile elements—the palatal muscles and their coverings—and this constitutes a breach in the naso-pharyngeal sphincter. Owing to the unopposed action of its muscles the soft palate is drawn both in a lateral and an anterior direction, and may thus appear unduly short.

Surgical Aims. Since the foundations of speech in the normal child are first laid during the second year of life, it is generally believed that cleft palates should be repaired when the child is about 15 months old. However, this argument is not universally accepted and some surgeons, anxious to avoid causing disturbances of growth by operative trauma, advocate a deliberate delay of 3 or 4 years. Whatever his preference, the surgeon should wait until growth of the parts is sufficiently advanced to make closure in a single procedure virtually certain, without such secondary ill-effects as retarded growth or serious alveolar distortion.

The aim of the surgeon is threefold: to close the gap by uniting both hard and soft palate in two layers in the midline; to mobilize the soft palate and shift it in a posterior direction, so that it reaches the posterior wall of the pharynx; and to avoid any disturbance of the muscular function of the palate, whether by scarring, tension, sepsis or direct damage to essential structures.

Operation. Endotracheal anæsthesia with a water-tight pharyngeal pack is essential. The best instrument for exposing the palate is the Kilner-Dott gag, a modification of the Davis-Boyle instrument.

The most useful procedure in the writer's opinion is the Wardill-Veau operation. When the cleft extends as far as the alveolus or nearly so, a four flap procedure as illustrated (Fig. 98) may be necessary, in spite of the obvious difficulties in mobilizing the small anterior flaps. However, in partial clefts of lesser extent, a simpler closure (using only the two posterior flaps) is sufficient, and this also applies where satisfactory closure of the anterior palate has been achieved at the initial lip operation.

The incisions are made as shown in the diagram. The muco-periosteal flap based on the posterior palatine artery is elevated on each side, exposing the free edges of the

palatal process, from which muscle and fascia are detached. The medial edges are either split or pared. The nasal mucosa on the upper surface of the bone, and on the vomer if available, is mobilized; a dissector is passed deeply beside the palatine artery over the medial surface of the internal pterygoid lamina, separating the mucosa from the bone. It has been a common practice to fracture the hamular processes medially. This is designed to release lateral tension and its effect is likely to be merely temporary.

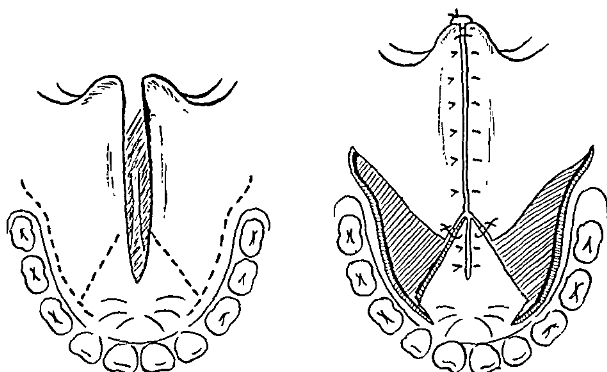


FIG 98. Incisions used for Wardill-Veau repair of palate. Note posterior advancement as well as median closure.
From "Cleft Lip and Palate" W G. Holdsworth, Heinemann)

When the anterior flaps and corresponding mucosa have also been mobilized, suturing is carried out in two layers. The nasal mucosa is repaired with catgut, the knots being tied on the nasal surface; the palatal flaps are then united and fixed so that the soft palate lies as far back as possible. A single suture from the nasal layer is left long and used to retain the mid portion of the palatal flaps in contact with the deep layer of nasal mucosa. If silk is used for the palate flaps it must be removed in 10 days and a general anæsthetic is necessary. Many surgeons prefer chromic catgut which can be left. In either case, "vertical mattress" sutures are advisable in order to obtain good apposition.

This operation leaves a considerable area of bare bone exposed, as well as two lateral cavities. To prevent the lodgment of food, some surgeons insert two packs soaked in Whitehead's varnish for 7 days. Healing of the raw areas is remarkably rapid.

The management of these cases is similar to that described in relation to cleft lip surgery, but in addition care must be taken to prevent remnants of milk feeds collecting along the suture lines. Each feed should end with a little water to wash the area clear of débris.

Complications. Reactionary hæmorrhage should only occur rarely, and is caused as a rule by damage to the palatine vessels, either at the foramen, or at the cut edge of the flap.

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muscular elevation parallel to Passavant's ridge but above it. This is achieved by raising a muco-muscular flap from the lateral pharyngeal wall on each side. These flaps are based upwards and are transplanted medially from a vertical to a horizontal plane. They contain palato-pharyngeus and other muscle elements, and when sutured in position side by side they establish both a muscular ridge and a secondary constriction of the nasopharynx. In expert hands this procedure has given impressive results.

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REGIONAL ASPECTS OF RECONSTRUCTION

NOSE

Two clinical groups of nasal defects may be distinguished as a matter of convenience; those with skin loss, and those with deformities of contour due to faults in the supporting bone and cartilage.

Skin Defects of the Nose

Skin lesions vary greatly in area and depth, and this has a direct bearing on the best method of repair. The smaller surface defects should be repaired by a free skin graft, unless the base of the raw area has an inadequate blood supply. Skin will "take" on any vascular tissue including nasal mucosa and perichondrium. The post-auricular skin is well suited to repairs of this kind, provided sufficient skin is available in this area.

When there is a full thickness loss with a nasal fistula, or where the base is avascular, skin with an independent blood supply must be introduced. The alternative means of carrying this out are described later under "Rhinoplasty."

Alar defects can as a rule be repaired with a composite auricular graft and this method may also be used for some columellar defects.

Rhinophyma may be treated surgically by paring the nose ruthlessly down to its

A breakdown of the suture line due to sepsis is unusual; it is apt to occur with babies in poor health, who may harbour hæmolytic organisms; a pre-operative nasal swab may give useful warning of this danger. Perforations should only occur in exceptional circumstances. The danger points are at the junction of hard and soft palate, where the nasal mucosa is easily torn; and at the junction of the four flaps, where accurate closure is difficult. A large posterior perforation or secondary cleft should, if possible, be repaired at a later stage. The secondary operation should if necessary be as extensive as the primary repair, rather than a niggling attempt at patch work.

It is often best to leave anterior perforations. They can be covered at any stage by an orthodontic appliance, and later by a partial denture which will probably be needed in any case with a difficult complete cleft. Surgical repair by local flaps should only be undertaken when the surgeon has good grounds for being confident of success.

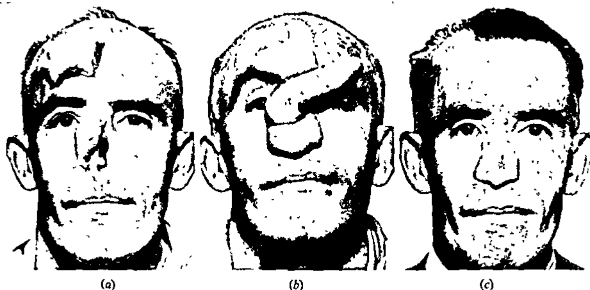
This introduces the subject of orthodontic control. It must at once be conceded that even the most skilled surgery will be followed in many instances by serious distortion of the alveolar (tooth-bearing) arch. The pre-maxilla may remain rotated, or may overlap the lateral part of the ridge; in other cases there may be a central collapse due to an inadequate bony "keystone." The advice and supervision of an orthodontic expert is invaluable, and it may be possible to start treatment at 4 years of age. In this way difficulties are prevented, and deformities regulated before they have become established.

Secondary Palate Operations. Patients are not infrequently seen, perhaps at the age of 8 or 12, who have had extensive surgery to the palate but with deplorable results in terms of normal speech. This faulty speech may be directly due to some degree of surgical failure. Apart from a fistula or partial breakdown the palate may be short, scarred, and immobile. While a skilled surgeon may be able to close a fistula, a repaired palate which remains short and rigid is a still more serious problem. Four types of procedure have been advocated. Firstly, attempts have been made to achieve a "push back," as suggested by Dorrance. Even when a free graft is inserted on the raw nasal surface this is a disappointing as well as a difficult procedure, since success must be judged solely by speech. Secondly, there is the Gillies-Fry operation which accepts a central defect at the junction of hard and soft palate, which can be closed by a dental obturator. This procedure consists of detaching the soft from the hard palate on each side, swinging it in a posterior direction, uniting the two halves centrally if they are cleft, and covering the raw edge with a Thiersch graft; this graft is applied on a gutta percha mould mounted on an adjustable dental appliance. It will be evident from this summary that this is not an entirely simple procedure. It is, however, a valuable solution to a particular type of problem.

Thirdly, difficult circumstances may justify a Rosenthal pharyngeal flap. In this operation, a flap is raised from the posterior pharyngeal wall, and turned forwards to join the short palate. A raw area is prepared on the latter to give a secure junction. The result of this procedure is to draw the palate towards the pharyngeal wall and to narrow the naso-pharyngeal opening. There are in effect two small separate openings, and this facilitates closure by the sphincter which is essential to normal speech. In the worst cases this procedure may be combined with a push back operation at a single session, and this manœuvre appears an important advance on the original Dorrance operation.

Lastly, Hynes has described a novel type of pharyngoplasty designed to produce a

In the first place the graft, shortly after it has been cut from the ear, is seen to be dead white, and in spite of the gentlest handling it is clear that virtually all blood has been expressed from it. The next phase is noted about 6 hours after the operation has been completed. The graft now has a pale pink tinge which is of uniform quality, there being no distinction between the colour of adjacent and remote areas. The third phase occurs at 12–24 hours. The graft is still uniformly coloured, but has now the blue-mauve tint described as "deep cyanosis." This cyanosis steadily clears until the graft acquires a healthy colour of excellent promise at a time varying between 3 and 7 days.



(*a*) (*b*) (*c*)

FIG. 100. Sir Archibald McIndoe's case.

(*a*) Patient with traumatic loss of nose showing preliminary design of lined forehead flap.
(*b*) Forehead flap during attachment.
(*c*) Final appearance with supporting bone graft.

It seems certain that successful ear grafts normally achieve an excellent blood supply within 5 days, and that the first colour changes must occur within 24 hours at the latest, unless necrosis is to follow. These early changes are a positive indication that erythrocytes have penetrated to a fairly uniform extent throughout the graft.

The raw edge of the nasal defect is (or should be) free from scar and highly vascular. The vascular bed in the ear is, apart from a narrow sliver of contained cartilage, one of the richest in the body. There are thus hundreds of arterioles, some of which might be expected to lie in favourable apposition. Provided a few of these vessels achieve continuity, entry of blood quickly follows and, with a rich and free anastomosis in the graft, the whole vascular bed should soon be filled. It is interesting to see that, as usual, the venous outflow does not keep pace with this inflow, and cyanosis is thus an invariable temporary state.

As regards clinical evidence of the earliest entry of blood, it may be mentioned that several surgeons with experience of ear grafts have noted definite colour changes (at least on isolated occasions) within 2 hours of grafting. It should not be assumed that this is usual or even desirable; but it is recorded as an observed phenomenon of some interest.

proper shape. It is often stated that no skin cover is needed, but in fact spontaneous spread of epithelium only occurs in certain cases. A free graft is usually required, but special attention must be paid to hæmostasis.

Auricular Grafts. The margin of the ear has certain obvious advantages for the plastic surgeon. It is easily accessible and simple to repair; it offers a "sandwich" of tissue consisting of two layers of skin with a contained layer of cartilage, while its general shape is similar to the alar margin. Above all, the auricular skin has a vascular bed which is one



(*a*) (*b*)

FIG. 99 Mr. J. Szlazak's case.

(*a*) Elderly patient with extensive alar defect following excision of carcinoma
(*b*) Repair by composite auricular graft

of the richest in the body, and this greatly encourages the establishment of a new circulation after transplantation.

The alar defect must first be defined accurately and a pattern cut in sterile tin foil. This is then laid on the most suitable portion of the rim of the ear, and the graft cut by transfixion. Any excess of cartilage is trimmed, and the graft is then fitted to the established defect (Fig. 99). The success of the operation depends on the raw edges of the defect having an adequate circulation to support the grafted tissue. Suturing is in two layers, uniting mucosa and skin with the finest catgut and silk sutures respectively. The graft should not be touched with forceps or hooks, but handled only by fingers covered with a gauze swab moistened with saline.

The subsequent history of these grafts and the development of their blood supply are of both clinical and academic interest, since certain biological processes are involved that are not solely confined to ear grafts. The condition of the circulation in the graft can be accurately assessed by the colour changes observed.

Congenital abnormalities should not be confused with the deformities due to inherited syphilis. An abnormal nasal contour, which is present early in life for no obvious reason, is liable to be labelled "cosmetic," and in this connection the surgeon must be on his guard against two opposite dangers. He should beware of the foolish or even psychotic individual with a nasal "fixation," who is convinced that his deformity is the cause of all his misfortunes. Equally he must guard against dismissing grotesque abnormalities of the nose as trivial. All patients, with whatever deformity, are entitled to be considered on their merits, and a ludicrous looking nose may be as embarrassing as a hairy mole or even a facial paralysis.

It should be mentioned that noses with large bony humps are unduly prone to injury, and it is often the accident which first brings the patient for advice. The operative treatment will be discussed later.

The earliest opportunity for *trauma* occurs during birth, and obstetrical injuries are by no means rare, though they are often overlooked. The most important injury of this kind is damage to the nasal bones or septum causing a saddle nose that may appear syphilitic. In a severe case, a graft may be indicated at the age of 5 or 6, and may require to be repeated, say at 12 and 18. The relative merits of bone and cartilage grafts are difficult to decide; but it must be remembered that bone of the desired bulk and texture is not easily obtained in the young, on account of the epiphyseal cartilage of the iliac crest.

Acute injuries of the nose are discussed on pp. 277 and 280. Apart from fractures, a septal hæmatoma may cause a collapse involving the lower part of the nose.

Old fractures which have not been properly reduced may result in serious deformities of contour as well as nasal obstruction. It is usually necessary to refracture the bones by saw or chisel. Section in four places is required, two at the apex and two at the bases of the nasal bones. If there is a bony hump the saw cuts along the bridge will be directed towards removing the redundant bone. This of course is also necessary in carrying out a nasal reduction, and must be accompanied by an "in-fracture." It is important that the basal saw cut should extend at least as far as (and immediately in front of) the inner canthus.

Remodelling of the lateral and alar cartilages may also be needed. This is ordinarily carried out through an inter-cartilaginous incision. The further details of nasal reconstruction are complex and variable and the curious reader is advised to consult the extensive special literature.

Collapse of the nasal contour may also result from a pyogenic abscess of the septum, from tuberculosis or from syphilis. Deformities due to simple sepsis are treated along similar lines to traumatic injuries.

The local effects of neoplasms and the associated problems of repair are discussed elsewhere A full-scale rhinoplasty is indicated for the more destructive nasal lesions. provided always that the primary disease is no longer active.

SCALP AND FOREHEAD

The repair of skin defects of the scalp and forehead is governed by special local conditions. The scalp is inelastic, and the wide undermining of ill-designed flaps pays poor dividends. Both scalp and forehead cover a convex surface and the inflexible laws of spherical geometry may involve unexpected difficulties in obtaining the necessary "advance."

Rhinoplasty. Extensive reconstruction of the skin surface of the nose is likely to require the operation of rhinoplasty. While this term might be held to include any plastic procedure of the nose, it is commonly used in this country only with reference to repair by local or transferred skin. A skin flap, with an intact blood supply may be introduced from the forehead; this is called a forehead flap, and is to be regarded as a special type of transposition flap moved in two stages (Fig. 100). It may be partly tubed. The design is a matter of importance, and it is essential that the distal portion of the flap, which may have to be turned in as a lining, should reach its new destination without that degree of torsion or tension which is likely to cause necrosis.



Fig. 101 Rhinoplasty by thoraco-acromial tubed pedicle; phase of attachment

Careful attention must thus be directed to the following points: the area of hairless forehead skin must be large enough to cover the defect; the length of the long curved incision in the hairy area of the scalp must be such as to give sufficient movement when the flap is mobilized; the main entering blood vessel, usually a branch of the superficial temporal artery, should be located and preserved; the galea should be taken with the scalp, except for the distal portion where it is left on the forehead; sepsis must be prevented by aiming at a "closed" operation, a free skin graft being applied to the whole donor area. Lining is obtained where possible by turning in local flaps from adjacent skin. If this is impossible, as it often is in total reconstruction of the nose, lining must be provided either by turning in the apex of the forehead flap (which is often impracticable), or by preparing a lining *in situ* on the forehead with a Thiersch or auricular graft. After an attachment of 18–21 days the unwanted portion of the flap is returned to the forehead, the superfluous area of skin graft being excised.

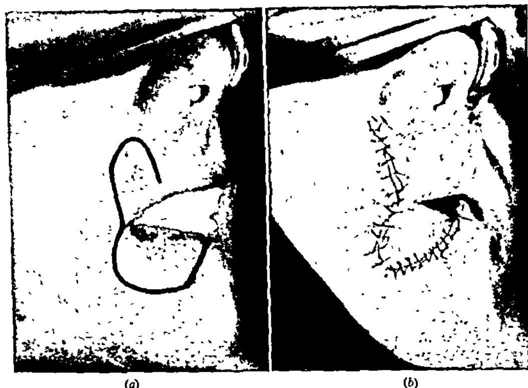
Occasionally it may be desirable at a later stage to support the reconstructed nose by a bone graft.

Rhinoplasty by tubed pedicle has certain advantages: it does not involve scarring of an exposed donor area; it provides a much larger maximum area of skin with which to make lining or columella; and it is the only alternative for patients who already have heavy scarring of the forehead. The pedicle may be brought up on the wrist from the abdomen and this involves four stages; but usually the three-stage thoraco-acromial type is preferred. It is then essential that the pedicle should be so designed that the upper end reaches as far as the point of the shoulder (Fig. 101). Rigid fixation during the period of attachment is not required, but restraint is essential and can usually be achieved with Elastoplast.

Defects of Contour

The causes of contour defects fall into the usual four categories: congenital, traumatic, infective, and neoplastic.

a distance; in deciding which is the method of choice in this area the surgeon should pay particular attention to the effect on appearance and expression. Skin grafts are apt to look patchy, but they may confer better expression in the area around the mouth than a thick, immobile pedicle. Local flaps may be the best compromise, and large defects can be covered by a well-planned and extensive advancement of tissue from the neck. Many



(a) (b)

Fig. 103 (a) Recurrent epithelioma of lower lip showing area of excision and design of Estlander flap.
(b) Flap in new position after transposition.

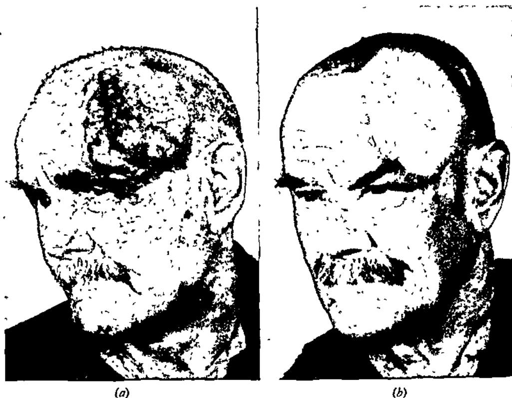
patients, especially in later life, have a considerable amount of surplus skin in the submandibular area, and Ferris Smith has shown how well this characteristic may be exploited.

Full thickness defects of the cheek may involve an oral or antral fistula. Lining is the principal difficulty, but extensive mobilization of the buccal mucosa may be accomplished by careful dissection; in cases where a hemiresection of the mandible is necessary, the additional gain in mucosa from the floor of the mouth may be great. Lesions involving the antrum may be treated as a modified Caldwell-Luc procedure, or in suitable cases the antral mucosa can be stripped and a formidable defect covered with an unlined forehead flap.

Occasionally a large compound lesion of the cheek, such as occurs in relation to carcinoma of the antrum, requires a large skin flap lined by an immediate Thiersch graft. In these cases this epithelial inlay must be supported by a suitable mould of gutta-percha or sponge rubber.

Major losses of lip tissue are treated in a number of ways, and in all possible instances by local flaps. The principal alternatives are three: an Estlander flap, transposed from the upper lip, will reconstitute as much as two-fifths of the lower lip (Fig. 103). The blood

The surgeon's object should be to achieve safe cover by preventing tension in the critical area, and free grafts should be reserved for what Gillies calls "areas of no importance." A rotation flap is nearly always the design of choice, and the incisions outlining this flap must be generously planned. It may be necessary for the area of the flap greatly to exceed the area of the defect, and it has been estimated that to advance the apex of a



(a) (b)

FIG. 102. (a) Epithelioma of temporal region.
(b) Primary repair by scalp rotation flap.

scalp rotation flap by 1 in. demands a curved incision 8 in. long, if the secondary defect is to be self-closing.

These problems only arise in defects with exposed bare bone, or some other avascular base. Free grafts may be used with confidence on galea or pericranium, and even (in exceptional circumstances) on bleeding cranium or dura mater. It should be mentioned that the straight-legged "tripod" incision for closing triangular scalp defects is futile, though it is frequently illustrated. Cushing's three-flap operation succeeds by virtue of the curve of its limbs.

The repair of large defects, especially those due to malignant disease, must be planned on a generous scale with no reservation as to secondary defects. A horseshoe shaped flap is often the most helpful design, its axis of movement is at right angles to its length, and it is easy to manipulate (Fig 102).

CHEEK AND LIPS

Defects in these areas can be divided into two groups: those with skin loss, and those that involve the full thickness of skin, muscle, and mucosa.

Large skin defects may be repaired by local flaps, free grafts or skin transferred from

Reference should here be made to the complex problem that arises when there is loss of eye, fornix, and lid. Infinite pains have been taken by many surgeons to reconstruct a satisfactory lid and socket, in the hope that the patient will be able to wear an artificial eye. Such efforts are seldom justified in the long run, and it may be best to close the defect and give the patient an external prosthesis which reproduces all the missing structures.

EARS

Plastic surgery to the ear is indicated in the following circumstances: for the repair of defects due to injury or disease, for reconstruction in congenital absence of the pinna (partial or complete), and for reduction of abnormally prominent ears.



FIG 104. Patient aged 6 with Treacher-Collins syndrome The profile and the ear deformity are both characteristic

Defects following injury or surgical excision may be complicated by a most painful chondritis, and this can often be avoided at operation by excising enough auricular cartilage to permit satisfactory suturing of the skin and thus provide safe cover.

Small defects such as those which remain after cutting a composite auricular graft can be closed by local skin with minimal deformity. Larger defects may need a direct skin

supply is carried on a tiny arterial pedicle. It is essential that the superior labial artery remains intact. The whole manœuvre is completed in one stage. The Gillies "fan-flap" is an ingenious—and characteristic—application of the same principle. It comprises the three layers of the cheek, but is highly unorthodox in that it is designed with an apex broader than its base. The latter carries an entering vessel from the arterial anastomosis near the corner of the mouth. The flap is rotated through as much as 180 degrees to lie in its new position. The secondary defect is closed by direct suture. The familiar rectangular design of Dieffenbach depends on swinging cheek flaps medially from both sides using all layers.

It will be seen that in each of these methods there are three layers—skin, muscle, and mucosa—which are mobilized as one, but are sutured in layers. The reconstitution of the oral sphincter is as important as skin replacement.

EYELIDS

Lesions of the eyelids involving loss of tissue have a serious effect on function, and carry a risk of conjunctivitis, epiphora or even corneal damage.

Treatment depends largely on whether the lid margin and tarsal plate are involved, and therefore lesions of the lids may be considered under two headings:

(1) Skin defects.

(2) Full thickness defects.

Skin defects require the introduction of new skin on a generous scale so that there is no pull on the lid margin and no impairment of mobility. The skin of the upper lid is extremely thin, and the pull of the levator palpebræ is insufficient to elevate a thick heavy lid. A thin split skin graft is the best choice for repairs of the upper lid and is applied on a "Stent" mould, after establishing the defect fully. On the other hand the lower lid is well served by a post-auricular graft, though in extensive skin loss involving lid and cheek a Thiersch graft is necessary. Minor degrees of ectropion due to paralysis or old age may be relieved by a lateral tarsorrhaphy, possibly reinforced by "advancement" of a skin flap. There are many variations of this manœuvre, but the principle is the same in each case, and depends on providing support, using skin as a sling.

Full thickness defects including loss of the whole lid may be exceptionally difficult to repair. These lesions seldom occur on the upper lid except in the form of a coloboma; this is a congenital gap in the skin and tarsal plate. Repair is usually carried out by mobilizing the two layers independently, with detachment (if necessary) of the tarsal plate from the lateral palpebral ligament. The tarsal plate and conjunctiva are sutured, care being taken that the knots will not rub against the cornea. The skin is then repaired, using an overlapping flap to avoid two coinciding and vertical suture lines.

Reconstruction of the lower lid depends on two alternative principles: either a rim of tarsal plate must be borrowed from the upper lid, and skin brought up from the cheek (Hughes' operation); or a bi-pedicled skin flap, usually known as a Tripier flap, may be cut from the upper lid and brought down to the lower, while lining is obtained by mobilizing the conjunctiva from the lower fornix as described by Manchester. This latter procedure is done in two stages, is not unduly difficult, and can be used in a majority of cases. The Hughes operation is of considerable complexity and difficulty and its details are outside the scope of this review. It may however be the only means of repairing a gross defect.

the post-operative management in terms of posture and movement, as well as bladder and bowel hygiene, must be given constant attention.

Chronic lymphœdema is a problem of great concern to physiologists and pathologists as well as surgeons, but many aspects of its nature are still obscure. Fortunately the methods of plastic surgery have a place in the treatment of selected cases. Watson has had success in treating patients with lymphœdema præcox, and his technique is briefly as follows: under a tourniquet the inner (or outer) aspect of the leg is flayed through a long mid-lateral incision. Two extensive skin flaps are turned back, these being cut so thin that they consist of skin and nothing else.

All fat and fascia is excised as far as the mid line both in front and behind. The skin flaps, although so thin, carry a considerable blood supply through the dermal capillaries; the marginal and less vascular portions of skin are treated like a Wolfe graft. As the dimensions of the leg are much reduced, it is usually possible to excise a considerable margin of redundant skin, thus reducing the size of the flaps. Multiple perforations are made to allow lymph and blood to escape. After releasing the tourniquet, the most careful hæmostasis is essential as even a small hæmatoma may produce necrosis. Massive dressings retained by broad crêpe bandages give the necessary support and immobilization is aided by a plaster of Paris backslab.

BREAST

Mammaplasty

Patients with gross deformities of the breast often endure a considerable degree of physical discomfort and mental distress. They may also suffer secondary ill-effects such as dorsal kyphosis and sub-mammary intertrigo.

Any classification of these deformities based on ætiology is bound to be arbitrary. Apart from cases of "virginal" hypertrophy, it is common to find that pregnancy appears to have played an important (and often repeated) role, and further trouble may follow attempted "slimming."

As the ætiology is apt to be complex and confused, it is better to adhere to simple descriptive categories. The patient herself will often use such terms as "drooping," "heavy," or "huge," and thereby usefully emphasize the features that trouble her. On this basis we can consider breast deformities under three headings:

(1) Ptosis—whether of large, small, or normal sized breasts.
(2) Hypertrophy—without ptosis.
(3) Asymmetry.

Indications for Operation. Mammaplasty must be considered on clinical rather than pathological grounds, though any suspicion of neoplasm must of course be excluded. If the patient's life is a physical burden or her condition is a source of not unreasonable depression, then her case should be viewed favourably. It is a wise precaution to explain to her that the operation of mammaplasty is a major one, and neither surgeon nor patient should embark on it lightly or unadvisedly.

Pre-operative precautions include an assessment of the hæmoglobin level, and arrangements for blood transfusion if this is likely to be required during operation; also local skin affections such as intertrigo must be eliminated as far as possible.

flap from the mastoid area. Major reconstruction depends on introducing cartilage, and this is a difficult procedure to bring to a satisfactory conclusion.

Preserved cartilage, cadaveric or bovine, may be carved to reproduce roughly the normal size and shape, but it is almost impossible to make an exact replica of the auricular cartilage in this way. More success has been obtained by filleting the mother's ear cartilage or by burying finely diced fragments of cartilage, contained in a two layered mould of metal or acrylic material, in the abdominal wall for 6 months.

In any case the new cartilage must be buried for some weeks under the post-auricular skin, before the new structure, skin and cartilage, is elevated from the deeper tissues through a posterior incision, and turned forwards. The retro-auricular defect, including the posterior surface of the new ear, is then covered with a Thiersch graft applied on a "stent" mould.

Complete absence of the external ear is uncommon, but a partial absence of a fairly standard pattern is often seen, and is associated as a rule with absence of the external auditory meatus, causing some deafness. This deformity is seen in a severe bilateral variation in the Treacher-Collins syndrome, where there is also a gross failure in growth of the mandibular rami, and other alterations in the facial skeleton (Fig. 104). Apart from cosmetic reconstruction of the pinna, a skin-lined tunnel to the mastoid antrum is necessary to produce an improvement in hearing.

Accessory auricles are frequently seen, usually just anterior to the meatus; they may also be encountered along a line from the ear to the mouth in the form of small cartilaginous nodules. A congenital sinus in the pre-auricular area may be first noted as a small abscess; a tiny dimple in the helix, near its junction with the cheek, confirms the diagnosis. A wide and careful dissection is necessary to eliminate all the ramifications.

Prominent ears may present such an abnormal and conspicuous appearance that surgical intervention is justified on social grounds. But it is well to remember that since the ear at the age of 7 is of almost adult proportions, it is apt to look unduly large, and some degree of temporary prominence at this age is very common. The ears may be surgically reduced using a posterior approach; a wide ellipse of skin is excised, exposing the cartilage near the outer margin. The line of the anti-helix, which is usually absent in these cases, is defined and marked. The cartilage is then incised along this line, and mobilized to a slight extent; the outer part is turned back at an acute angle to form the anti-helix (and sometimes the superior crus). It is held thus by mattress sutures of catgut. The closure of the skin defects acts in some measure as a splint.

LOWER LIMBS

The applications of plastic surgery to traumatic and other lesions of the legs are so extensive, that only a summary can be given. Many of the problems are closely related to the field of orthopædic surgery, where sound skin cover is essential for secondary bone operations. The cross-leg flap is ideal for these cases (q.v.). This procedure is also useful in selected cases of osteomyelitis, delayed union, and traumatic ulceration.

The paraplegic patient may develop decubitus ulcers, involving the lower limbs as well as the sacrum, iliac crest and ischium. The more serious and extensive ulcers are likely

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Pre-operative precautions include an assessment of the hæmoglobin level, and arrangements for blood transfusion if this is likely to be required during operation; also local skin affections such as intertrigo must be eliminated as far as possible.

Operation. The standard procedure was derived by Gillies and McIndoe from Biesenberger, and is a one stage operation which makes use of a pedicle of breast tissue including the nipple.

Alternative techniques include a two stage reduction of each breast: or operation on one side at a time: or transplantation of the nipple and areola as a free graft. For patients



FIG 105 Patient with hypertrophy of right breast; appearance after reflection of skin flaps and before excision of gland tissue.

with enormous hypertrophy, or the elderly, these other methods may be worthy of consideration.

The standard operation is applicable to a large majority of patients and its principal steps are as follows.

The patient is placed on the table with the upper half of the body tilted by 30–45 degrees above the horizontal. Two marks in sterile ink are made, one at the sternal notch and the other over the xiphisternum. The new site for the nipple is selected with due regard to the patient's age and habitus, but it will commonly lie 7½ in. from the upper mark and 5 in. from the lower one. A circle about 2 in. in diameter is then drawn round the nipple, and finally a line is carried from the top of the circle to the new nipple site, and from its lower edge vertically downwards. Following these marks incisions are made, and the lateral skin flaps are reflected from the breast. The plane of dissection is very superficial at first but as it extends the skin flaps should be cut about ⅛ in. thick. When this procedure is complete the breast will hang freely, denuded of skin but suspended by its own vascular pedicle (Fig. 105) By a curved incision on its outer aspect, the unwanted gland tissue and fat are excised, leaving a pedicle supplied by branches of the internal mammary artery.

The lower end of this pedicle is turned outwards and upwards—through 180 degrees—and provisionally sutured to its base, so that the nipple lies at its correct new level.

The skin flaps are then draped over the reduced breast and held with a light curved intestinal clamp; this produces the correct elevation and thus provides the proper skin tension. Marks are drawn in ink along the curve of the clamp and the excess of skin is

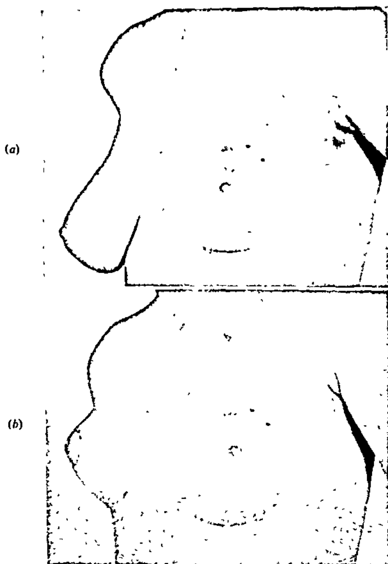


FIG 106. (*a* and *b*) Same patient before and after mammaplasty to the right side.

excised. Preliminary suturing of the skin edges for a distance of 3 or 4 in. from above downwards indicates a further excess of skin near the chest wall. This is marked and excised as a horizontal ellipse to give a long curved suture line lying in the sub-mammary fold. A suitable circle is then cut at the upper end of the vertical suture line to receive the nipple, and the areolar margin is sewn into position.

Hæmostasis and gentle handling are imperative. Drains are advisable. Dressings must be massive and securely maintained, a many-tailed crepe bandage offers the best fixation.

Post-operative care is directed towards maintaining the correct fluid and hæmoglobin levels, and thus avoiding post-operative shock and local ischæmia. Complications include hæmatoma, necrosis of skin margins or of nipple; but these—together with ill-designed contours and poor symmetry—should not be seen too often after an operation by a competent plastic surgeon (Fig. 106).

There can, however, be few procedures in which surgical inexperience involves a stronger probability of disastrous consequences.

Gynæcomastia

Abnormal hyperplasia of breast tissue in the male is a rare but embarrassing condition. It is frequently unilateral. Although gynæcomastia is usually first noticed at puberty, it seldom responds to hormone therapy.

Surgical treatment is indicated for patients with persistent breast enlargement which is unrelated to any obvious testicular abnormality. An incision is made along the outer part of the sub-mammary fold, and by undercutting with scissors, the gland is extirpated leaving the nipple intact. Bleeding is brisk and direct hæmastasis difficult. Drainage and firm dressings should prevent collection of a troublesome hæmatoma.

PHARYNX

Repair following Pharyngo-laryngectomy

In cases of cancer the onus of closing the formidable defect which follows total excision of the larynx, together with a considerable portion of the pharynx, may fall on the reconstructive surgeon, either at the original operation or as a secondary procedure.

In essence it is necessary firstly to achieve an anastomosis between the open pharynx above and the divided end of the œsophagus below, and secondly to provide satisfactory skin cover. Though preliminary manœuvres may sometimes be necessary, these two tasks must finally be completed at a single operation. The situation is often complicated by an awkwardly placed tracheotomy opening, or by a troublesome zone of intractable dermatitis due to irradiation therapy. Further technical problems are related to the poor blood supply of the œsophagus, the presence of saliva which is seldom effectively reduced by drugs, the age and frailty of many of the patients, the difficulties of immobilization, and the uncertain prognosis which may exclude an elaborate programme of multi-stage procedures.

Technique of Secondary Repair. Unless there is an ample strip of pharyngeal mucosa, it is necessary to turn hinged skin flaps in from each side to provide an epithelial lining. If these flaps have been subjected to heavy irradiation, the greatest care and judgment are needed to prevent sloughing from ischæmia after the flaps are undermined and turned in. Skin cover must be generous It is seldom wise to use the ⌶ -shaped incision with lateral advancement flaps, as frequently advocated, since tension and sloughing are likely to occur. The best and safest design here (as in many other comparable situations where a marginal breakdown is fraught with dire consequences) involves the use of two large rotation flaps; these are marked out in ink—one based above near the ear, and the other below near the clavicle. These two flaps, ascending and descending, should give secure cover without tension or ischæmia. They will meet each other obliquely, thus avoiding overlying suture lines.

Aftercare includes the use of an oiled silk apron around the tracheotomy tube, as it is essential to protect the flap margins from mucous discharges. Regular aspiration of accumulated mucus from the trachea by a soft rubber catheter is needed. Saliva should be ejected rather than swallowed. Feeding is usually carried out by an œsophageal plastic tube passed through the nose. This should be of reasonably fine calibre bearing in mind that, with feeding, quantity rather than speed is important.

URETHRA

Hypospadias

This deformity results from a failure of ventral closure of the male urethra and varies greatly in degree. It must be distinguished from the much rarer condition of "congenital short urethra," in which there is chordee due to shortage of tissue on the ventral aspect, but the meatus is in the normal position. The usual classification of hypospadias is based on the site of the displaced meatus and is as follows:

(1) Coronal.
(2) Penile.
(3) Peno-scrotal.
(4) Perineal.

The exact category may appear largely an academic issue, but it is most important to be able to advise parents on prognosis according to the severity of the deformity. The prognosis is also related to the degree of chordee which may sometimes be serious even in apparently minor cases of hypospadias.

In deciding whether to operate the surgeon is concerned with providing normal urinary and sexual function. If there is no obvious—or latent—ventral chordee, and if the urinary stream can be properly directed when the patient is standing, then the indications for operation will be based less on surgical than on æsthetic grounds. On the other hand, chordee should always be corrected early to prevent difficulties in sexual intercourse, and a child's urethra which opens $\frac{1}{2}$ in. or more from the correct site requires to be extended surgically, as it may cause urinary embarrassment, and even sterility—though not impotence.

Operative Plan. Chordee is best corrected at about 18 months. The simplest procedure—and in most cases the best—involves a single transverse incision just distal to the meatus; this gives access to the fibrous band which appears part of the corpus spongiosum and which causes the ventral kinking; after the necessary excision, which must be performed with great exactitude, the meatus will tend to move in a proximal direction, as the kinking is released. Closure depends on mobilizing the local preputial skin, and the wound is finally sutured in a longitudinal axis. If the meatus is unduly small, a meatotomy is required, mucosa being united to skin by tiny catgut sutures. The wound is not adversely affected by the passage of urine through the adjacent meatus.

The second stage of repair, namely reconstruction of the terminal urethra, should be capable of completion by the time the patient is 5 years of age, prior to his going to school. This ideal is best fulfilled by the Denis Browne operation; his method represents a *major* advance in urethral surgery and depends for its success on several factors; these include the "reservoir" of suitable skin in the preputial hood, the tendency of any track lined with epithelium to remain open, and the fact that penile skin does not form keloid scars. The

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The exact category may appear largely an academic issue, but it is most important to be able to advise parents on prognosis according to the severity of the deformity. The prognosis is also related to the degree of chordee which may sometimes be serious even in apparently minor cases of hypospadias.

In deciding whether to operate the surgeon is concerned with providing normal urinary and sexual function. If there is no obvious—or latent—ventral chordee, and if the urinary stream can be properly directed when the patient is standing, then the indications for operation will be based less on surgical than on æsthetic grounds. On the other hand, chordee should always be corrected early to prevent difficulties in sexual intercourse, and a child's urethra which opens ½ in. or more from the correct site requires to be extended surgically, as it may cause urinary embarrassment, and even sterility—though not impotence.

Operative Plan. Chordee is best corrected at about 18 months. The simplest procedure—and in most cases the best—involves a single transverse incision just distal to the meatus; this gives access to the fibrous band which appears part of the corpus spongiosum and which causes the ventral kinking; after the necessary excision, which must be performed with great exactitude, the meatus will tend to move in a proximal direction, as the kinking is released. Closure depends on mobilizing the local preputial skin, and the wound is finally sutured in a longitudinal axis. If the meatus is unduly small, a meatotomy is required, mucosa being united to skin by tiny catgut sutures. The wound is not adversely affected by the passage of urine through the adjacent meatus.

The second stage of repair, namely reconstruction of the terminal urethra, should be capable of completion by the time the patient is 5 years of age, prior to his going to school. This ideal is best fulfilled by the Denis Browne operation; his method represents a major advance in urethral surgery and depends for its success on several factors; these include the "reservoir" of suitable skin in the preputial hood, the tendency of any track lined with epithelium to remain open, and the fact that penile skin does not form keloid scars. The

Post-operative care is directed towards maintaining the correct fluid and hæmoglobin levels, and thus avoiding post-operative shock and local ischæmia. Complications include hæmatoma, necrosis of skin margins or of nipple; but these—together with ill-designed contours and poor symmetry—should not be seen too often after an operation by a competent plastic surgeon (Fig. 106).

There can, however, be few procedures in which surgical inexperience involves a stronger probability of disastrous consequences.

Gynæcomastia

Abnormal hyperplasia of breast tissue in the male is a rare but embarrassing condition. It is frequently unilateral. Although gynæcomastia is usually first noticed at puberty, it seldom responds to hormone therapy.

Surgical treatment is indicated for patients with persistent breast enlargement which is unrelated to any obvious testicular abnormality. An incision is made along the outer part of the sub-mammary fold, and by undercutting with scissors, the gland is extirpated leaving the nipple intact. Bleeding is brisk and direct hæmastasis difficult. Drainage and firm dressings should prevent collection of a troublesome hæmatoma.

PHARYNX

Repair following Pharyngo-laryngectomy

In cases of cancer the onus of closing the formidable defect which follows total excision of the larynx, together with a considerable portion of the pharynx, may fall on the reconstructive surgeon, either at the original operation or as a secondary procedure.

In essence it is necessary firstly to achieve an anastomosis between the open pharynx above and the divided end of the œsophagus below, and secondly to provide satisfactory skin cover. Though preliminary manœuvres may sometimes be necessary, these two tasks must finally be completed at a single operation. The situation is often complicated by an awkwardly placed tracheotomy opening, or by a troublesome zone of intractable dermatitis due to irradiation therapy. Further technical problems are related to the poor blood supply of the œsophagus, the presence of saliva which is seldom effectively reduced by drugs, the age and frailty of many of the patients, the difficulties of immobilization, and the uncertain prognosis which may exclude an elaborate programme of multi-stage procedures.

Technique of Secondary Repair. Unless there is an ample strip of pharyngeal mucosa, it is necessary to turn hinged skin flaps in from each side to provide an epithelial lining. If these flaps have been subjected to heavy irradiation, the greatest care and judgment are needed to prevent sloughing from ischæmia after the flaps are undermined and turned in. Skin cover must be generous It is seldom wise to use the ⌶ -shaped incision with lateral advancement flaps, as frequently advocated, since tension and sloughing are likely to occur. The best and safest design here (as in many other comparable situations where a marginal breakdown is fraught with dire consequences) involves the use of two large rotation flaps; these are marked out in ink—one based above near the ear, and the other below near the clavicle. These two flaps, ascending and descending, should give secure cover without tension or ischæmia. They will meet each other obliquely, thus avoiding overlying suture lines.

is kept dry and powdered, and it is essential to avoid kinking especially at the peno-scrotal junction.

The catheter is withdrawn at 7 days, and the tension sutures are cut and removed at about the same time. The perineal fistula should then close spontaneously within a few days. It has been found that the circumference of the new urethra is at least 30 per cent greater than the width of the original strip of epithelium. It is also noteworthy that as the child develops the reconstructed urethra grows in direct proportion to related structures.

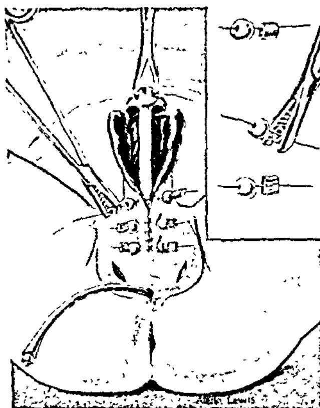


FIG 108 Apposition of lateral flaps using nylon sutures, beads and aluminium cylinders The fine midline sutures are usually inserted afterwards (*Post-grad J. med*)

References

Regional.

Nose.

Brown, J. B. and McDowell, F. (1951) "Plastic Surgery of the Nose." *Henry Kimpton*, London.

Scalp·

Gillies, H. D. (1944) "Note on scalp closure." *Lancet*, ii, 310.

Ears·

Jayes, P. H. and Dale, R. H. (1951) "The treatment of prominent ears." *Brit. J. Plast. Surg.* 4, 193.

Eyelids

Hughes, W. L. (1943) "Reconstructive surgery of the eyelids." *Henry Kimpton*, London.

Manchester, W. M. (1951) "A simple method for the repair of full-thickness defects of the lower lid with special reference to the treatment of neoplasms." *Brit. J. Plast. Surg.* 3, 252.

Schofield, A. L. (1954) "A review of burns of the eyelids and their treatment." *Brit. J. Plast. Surg.* 7, 67.

Lower Limbs

Battle, R. J. V. (1949) "Pressure sores in paraplegic patients." *Brit. J. Plast. Surg.* 1, 268.

Watson, J. (1953) "Chronic lymphœdema of the extremities and its management." *Brit. J. Surg.* 41, 31.

only reasonable criticism of the method is that a perineal urethrostomy is obligatory. However, this does not seriously prolong the operation or disturb the patient, provided it is skilfully carried out.

Operative details are briefly as follows: A Malecot catheter on a sound is introduced into the bladder. The sound is then partly withdrawn, rotated through 180 degrees and made to present under the perineal skin. Using (for choice) a diathermy needle, the

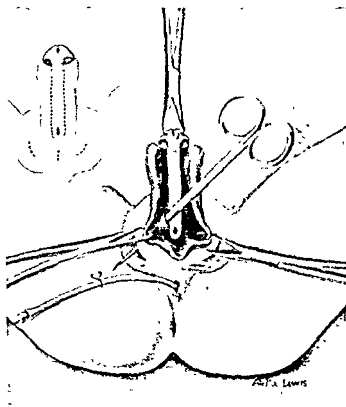


FIG. 107 Drawing to show central epithelial strip and lateral skin flaps (*Post-grad J med*)

catheter is exposed and the outer end is drawn out through the wound. It is anchored here by a silk stitch.

A strip of skin about 8–10 mm. in width is then outlined on the ventral surface of the penis. This is U-shaped, embraces the meatus, and at its distal end on each side includes the edge of the glans which must be denuded of epithelium. This strip is not undermined, but the two lateral skin flaps are widely mobilized (Fig. 107). A longitudinal relaxation incision is made along the dorsum of the shaft. The lateral flaps can then be sutured together in the midline, thus burying the central strip. An exaggerated degree of apposition is necessary and this is accomplished by four or five strong nylon tension sutures. The ends of these are not tied, but carry a bead and aluminium "stop" on each side which control the skin flaps, and maintain full eversion (Fig. 108). Simple sutures are inserted to unite the actual edges, and to fix the distal margin to the prepared areas on the glans.

After operation it is usual to discontinue all dressings within a few hours. The wound

flaps is relatively rare and marginal trimming should be minimal. Primary suture, whether immediate or delayed, should seldom fail to achieve satisfactory healing by first intention, unless there is a considerable loss of tissue.

Although injured patients often appear to be suffering from serious loss of tissue, these defects may be due to retraction of the skin edges and may be more apparent than real. Even where true loss of skin has occurred it is often possible, with a little patience and ingenuity, to obtain closure without tension by a discreet use of local flaps. Free grafts are only indicated as a second choice.

Surface abrasions, commonly involving the upper lip or malar region, may present an awkward problem. The primary duty of the surgeon is to remove from the raw surface all ingrained dirt to prevent a grey tattoo; for this purpose curetting with a steel spoon may be obligatory. In spite of this double damage, satisfactory early healing usually occurs as with the donor area of a Thiersch graft.

Full thickness injuries, especially of the lips, must be repaired in their appropriate layers; accurate apposition of a muscle layer is just as important as careful suturing of the skin.

In severe penetrating wounds, with gross loss of substance including skin, muscle, and mucosa, no attempt at primary repair under tension should be made. These wounds, common in wartime but fortunately rare among civilian injuries, are treated by suturing skin to mucosa around their periphery; the defect thus established is then closed at a later date by a carefully planned procedure, possibly in multiple stages.

Lacerations of the skin, which are often found in relation to comminuted nasal fractures, should be repaired first before proceeding to reduce the nasal bones. This avoids extrusion and further external contamination of the bony fragments.

FACIAL FRACTURES

It is convenient to consider facial fractures on a regional basis. That part of the skeleton which lies between the frontal bone and the mouth is known as the middle third of the face, and bony lesions occurring here are commonly called "middle third fractures." Fractures above this area are frontal and those below are mandibular.

Middle Third Fractures

The anatomical structure of the facial skeleton is highly complex, and unless bony injuries are considered on a systematic basis it is difficult to explain or understand the commoner lines of fracture and the related complications.

Maxillary Fractures. A convenient classification, adopted by Moore and Ward, is as follows (Fig. 110):

(1) High Transverse Fracture. This involves a high level separation between the facial bones and the skull. The line of fracture runs through the upper portion of the nasal and ethmoid bones and across the orbit on each side.

(2) Pyramidal Fracture. The apex of the fracture line starts at the nasion, crosses the antra obliquely below the malar bone on each side and ends in the pterygoid region.

(3) Low Transverse Fracture. This is known as a Guérin fracture. It involves a separation of the tooth-bearing alveolus from the upper part of the maxilla. The fracture runs horizontally at the level of the nasal floor.

Breast:
McIndoe, A. H. (1950) "Techniques in British Surgery." Edited by R. Maingot, *W. B. Saunders*, London, p. 264.
Pharynx:
Moore, F. T. and Faulkner, T. (1953) "Repair following pharyngo-œsophagolaryngectomy." *Brit. J. Plast. Surg.* 6, 102.
Urethra:
Browne, D. (1949) "Hypospadias." *Post-grad. J. med.* 25, 367.

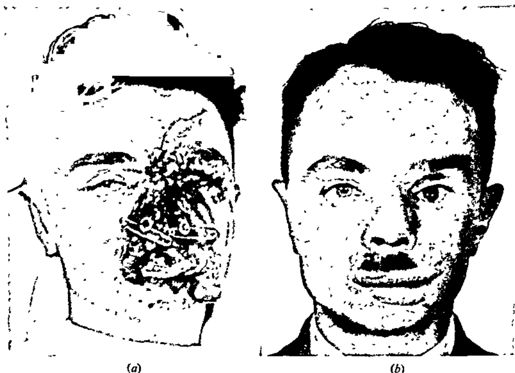
MAXILLO-FACIAL INJURIES

Introduction

Injuries of the face and jaws may involve either bone or soft tissues, or both. In certain respects fractures of the face may be considered similar to bony injuries to the limbs. Thus it is possible to classify them as "closed" or compound, and to describe them as simple, comminuted, or impacted. Every kind of combined injury is also encountered, and closed fractures may occur at the same time as soft tissue lacerations which are not directly related to them.

Soft Tissue Injuries

The skin and soft tissues of the face have a phenomenally rich blood supply, and this factor greatly influences the treatment of facial lacerations (Fig. 109). Necrosis of skin



(*a*) (*b*)

FIG 109 Sir Archibald McIndoe's case.

(*a*) Severe compound injury of face due to contact with aircraft propeller.
(*b*) Patient following reconstruction which included rhinoplasty.

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Urethra.
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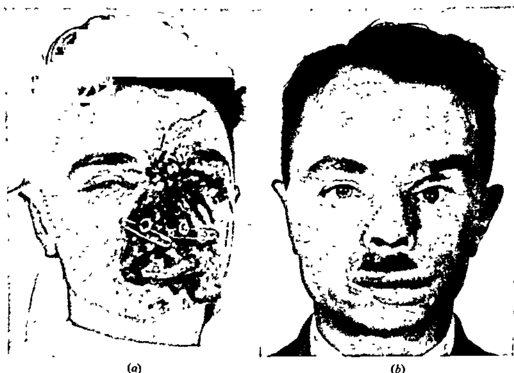
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(*a*) (*b*)

FIG 109. Sir Archibald McIndoe's case

(*a*) Severe compound injury of face due to contact with aircraft propeller.
(*b*) Patient following reconstruction which included rhinoplasty.

(4) Vertical Fracture. This involves separation near the midline between the two halves of the maxilla. It is often associated with a unilateral Guérin fracture or a more extensive comminution.

It must be emphasized that neither this or any other classification is to be regarded as a rigid system; there can be many minor variations, as well as complex composite fractures. It should, however, be noted that the "classical" lines of fracture all tend to follow the line of least resistance, where the structure of the bony skeleton is weakest.

Nasal Fractures. The nasal bones may be fractured either as part of a middle third fracture, or as an isolated injury. Every untreated nasal fracture carries a risk of probable deformity, with possible obstruction to the nasal airways. Reduction should be carried out after any fractures to adjacent bones that have been reduced. It must be remembered that the deformity of the nasal septum which is often present is apt to persist in spite of proper bony reposition, and the need for a sub-mucous resection at a later stage cannot always be prevented.

Malar Fractures. Injuries to the malar bone may be associated with fractures of the maxilla, but are often seen alone; they are sometimes called "lateral middle third" fractures. When there is much displacement of the malar bone the zygomatic process of the temporal bone is usually fractured with collapse of the arch. The relationship of the malar bone to the orbit above and the antrum below is of great importance. But apart from damage to these cavities, all displacements of the malar bone affect the contour of the cheek, producing a characteristic asymmetry of the face; the bone may also impinge on the coronoid process of the mandible, either causing a secondary fracture or interfering with the movements of the jaw.

Fractures of the Mandible

The mandible is frequently fractured without any associated injury to other structures. The cause may be either direct or indirect violence; fractures of the tooth-bearing portion are likely to be compound, due to tearing of the mucosa; on the other hand fractures of the condyle neck or the ascending ramus, where the force responsible is often transmitted indirectly, are usually closed. In many instances there is a double or triple fracture, due to a combination of direct and indirect violence.

The most urgent primary problem in fractures of the mandible arises from the patient's inability to control his tongue. When the mandibular attachment of the lingual muscles is displaced backwards, the pharynx may easily become obstructed, particularly if there is considerable intra-oral bleeding.

The later complications of a malunited fracture of the mandible are mainly due to faulty dental occlusion.

Local Complications of Facial Fractures

The various complications associated with facial fractures may be usefully considered according to the regions involved. Some of these ill-effects are observed temporarily during the acute phase, in spite of correct treatment, some are seen later, and their incidence is likely to depend on the competence of the early treatment; but some complications are unavoidable. Many of these sequelæ, however, can be relieved or mitigated by well-planned secondary procedures.

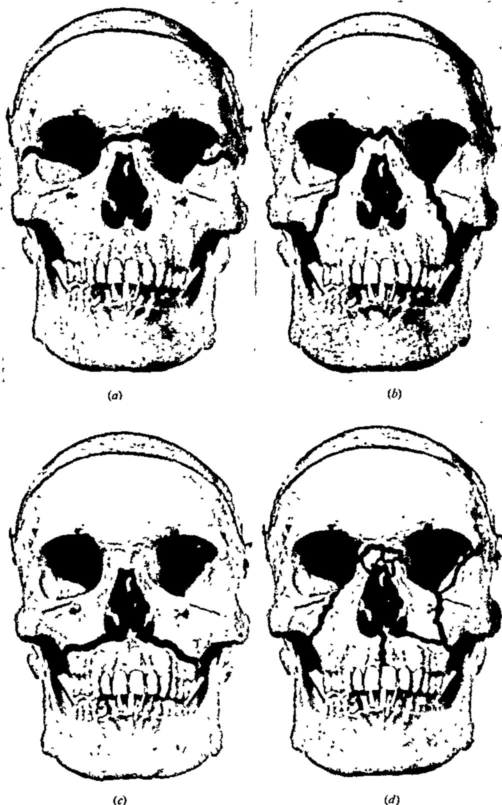


FIG 110 Diagrams of middle third fractures showing·
(a) High transverse fracture
(b) Pyramidal fracture.
(c) Low transverse fracture
(d) Multiple bony injuries including vertical fracture

fracture work. Inter-maxillary fixation (I.M.F.), oral hygiene, and many related questions of management should not be left to the general or the plastic surgeon.

For these reasons only the simplest summary of principles will be given concerning the treatment of fractures of the maxilla and mandible.

First-aid measures are devoted to controlling bleeding, removing clots and mucus

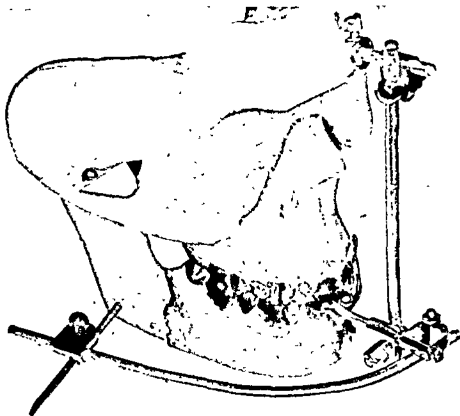


Fig 111. Model demonstrating combined fixation using upper and lower metal cap splints, plaster headcap, and external pinning.

from the mouth, and maintaining a safe airway. The effects of gravity must be used for the patient's advantage. The conscious patient should sit in bed with his head slightly forwards; if unconscious he should be placed flat in a semi-prone position, and kept under close supervision.

Provisional support by a crêpe "barrel" bandage is useful, but it must be so placed that the lower jaw is held in occlusion and not displaced backwards. The four-tailed bandage, which so frequently figured in older books, should therefore never be used.

Reduction is often quite simple, but can be extremely difficult. The maxilla may be firmly impacted, and all efforts must be devoted towards mobilizing it. Only occasionally is skeletal traction necessary.

Immobilization depends, in principle, on securing at least one fixed point, and, in particular, on the security conferred by metal cap splints cemented on to the teeth. Dental wiring is seldom so satisfactory as rigid splints.

Nasal complications have been mentioned already and include disturbances of profile, lateral deviations, and obstructed airways.

Sinus complications are less common than might be expected; distortions of the shape and size of the air sinuses are frequently seen, but seldom give rise to serious chronic inflammation.

Alveolar complications include every kind of malocclusion. Even small disturbances of "bite" are embarrassing to the patient. Nor can it be assumed that small dental adjustments will easily cure these faults. It must also be remembered that the edentulous patient may suffer serious inconvenience from malocclusion in spite of modified dentures.

Contour changes may be evident even to a casual observer. The varieties most frequently seen include depression of the cheek, recession of the upper jaw, alterations of the nasal bridge, collapsed frontal sinuses and mandibular distortion.

Orbital complications include alterations of the bony orbit, as well as damage to the globe and lacrimal apparatus. Gross violence may cause rupture of the globe or injury to the optic nerve. Downward displacement of the globe is due not to depression of the floor of the orbit, but to interference with the supporting "check" ligaments and their bony attachments. Loss of orbital fat may cause enophthalmos. These alterations in the position of the globe frequently produce transient or permanent diplopia. Damage to the levator muscle of the upper lid or to the canthal ligaments may cause ptosis or alteration of the palpebral fissure.

Intra-cranial complications are outside the scope of this chapter, though due regard must be paid to any significant features such as cerebro-spinal rhinorrhœa. It is, however, noteworthy that in general the face "protects" the brain, and cerebral injuries are a less frequent complication of facial injuries than might be expected.

Diagnosis of Facial Fractures

It is imperative that any patient with injuries likely to include a facial fracture should if possible be examined by an expert dental surgeon. Disturbances of "bite" are not always easy to recognize, but are often the main indication of a maxillary or a mandibular fracture. In addition a careful inspection of the contours of the face must be made, with special regard for asymmetry. The stability of the maxilla should be tested manually. A digital examination should include the orbital margins, the condyles of the mandible (in open and closed positions), the malar-zygomatic prominences and the body of the mandible. Intraoral bleeding is important as evidence of a probable fracture.

Appropriate X-rays will give accurate information, but should be taken after and not before a full clinical examination. It must not be forgotten that a careful history may give suggestive or conclusive evidence on certain doubtful points.

Treatment of Facial Fractures

After diagnosis, the essential steps in treatment are:

(1) Reduction.

(2) Immobilization.

Fractures of the mandible and maxilla (apart from nasal and malar injuries) almost always involve problems of dental occlusion. Their general treatment, and in particular their immobilization, should emphatically be supervised by a dental surgeon trained in

Treatment of Malar Fractures

A depressed malar fracture requires prompt elevation. A careful clinical examination, and a study of the X-rays will show the precise nature of the deformity. The surgeon should determine by palpation whether there is a step deformity in the infra-orbital margin, or a gap near the fronto-malar suture just above the outer canthus.

In the majority of cases the malar displacement can be reduced from above by the temporal approach of Gillies. This manœuvre relies on the anatomical plane between the temporal fascia and zygomatic arch on the one hand and the temporalis muscle on the other. A small temporal incision is made dividing skin, galea and both layers of the temporal fascia. Through this opening a heavy elevator is passed which can then be made to slide without difficulty or trauma under the lateral edge of the malar. Powerful elevation will correct the deformity and the bone is often heard to "snap" into its proper position (Fig. 112).

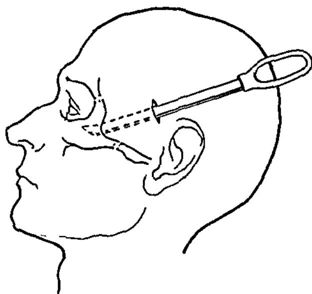


FIG. 112. Diagram showing elevation of fractured malar bone by superior approach.

If, however, the malar displacement is mainly in a downward direction with collapse of the antrum, a Caldwell-Luc approach through the upper buccal sulcus is advisable. In all correctly selected cases a defect will be found in the antral wall, through which a finger or elevator can be inserted. Great care must be exercised to avoid damage to the eye through the antral roof. After reduction of the malar deformity and expansion of the antral cavity to its proper size, the latter is packed firmly with ribbon gauze soaked in Whitehead's varnish; several yards may be required.

In difficult cases a combined approach by both methods may be needed before reduction is satisfactory. External fixation is seldom required, except in rare fractures which are unstable after reduction. Direct wiring, however, has certain definite indications; it is of particular assistance in reducing fractures where there is a bony gap at the outer canthus complicated by diplopia. This gap should be exposed by a direct approach and defined; holes are then drilled in the adjacent bone and after the fracture has been mobilized by another route, exact fixation is achieved by a single strong wire suture.

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Rowe, N. L. and Killey, H. C. (1955) "Fractures of the facial skeleton." *Livingstone*, Edinburgh.

The intact maxilla is naturally the best fixation point for the fractured mandible; conversely a fractured maxilla can be held in position by the intact mandible and further secured by external rods fixed to a plaster headcap.

Where teeth are absent or insufficient, it is often necessary to use two acrylic alveolar splints; these upper and lower Gunning's splints are retained by wires which encircle the upper alveolus and mandible respectively.

In fractures of the neck of the condyle on one side, the position of normal occlusion must be obtained without delay, and cap splints are usually needed for a few days only. The exact reduction of the upper fragment—that is, the condyle itself—and the achievement of bony rather than fibrous union are both relatively inessential.

When both condyle necks are fractured, early exact reduction of the *main body* is imperative to avoid an "open bite."

Extra-oral fixation may be indicated in addition to, or instead of, intraoral fixation. An orthopædic pin is then inserted through the skin to transfix the uncontrolled bone which is usually a posterior fragment of the mandible without teeth (Fig. 111). Alternatively, direct wiring of the upper border of the mandible may be indicated to control an edentulous fragment. Similarly lower border wiring is often used in relation to compound mandibular injuries where the line of fracture lies at the bottom of an external wound.

During the period of 3 weeks or longer while the jaws are immobilized, hygiene and adequate calorie intake are of paramount importance. A diet of 1,500 calories a day is required and must be either fluid or semi-fluid. However, these vital matters, in which dental supervision is essential, cannot be appropriately dealt with here, and the reader is referred to the special literature dealing with these problems.

Treatment of Nasal Fractures

Reduction of nasal fractures should be carried out under endotracheal anæsthesia Associated injuries such as concussion may justify a delay of a day or so, but as time passes the mobilization of the fracture becomes more formidable, and after 14 days is impossible by simple measures.

The bone on each side is disimpacted by Walsham's forceps (or a similar instrument), with one blade inside the nose and the other, covered by rubber, in contact with the skin of the side of the nose. At the same time digital control of the fragments is necessary to prevent splaying of the bridge due to lateral displacement of the fragments towards the orbit. The bony septum is manipulated by Asch's forceps.

Unless the fractures are trivial, splinting is required. A thin slab of plaster, broad on the forehead and shaped over the nose, is useful. If there is gross comminution with collapse, more elaborate measures may be required. Careful packing of the nasal cavities with petrolatum gauze is the safest method of maintaining the airways, but it will be obvious that excessive packing may further displace the nasal bones. In addition rigid lateral support may be needed to maintain the profile. In these cases two oval lead plates, 1½ in. long, are cut—each with two small holes. These plates are moulded and held against the sides of the nose by a wire. This, mounted on a straight needle, is pushed through the upper hole of one plate, and then (via the fracture lines) right through the nose. It emerges through the opposite plate, and returns via the lower holes. The ends are twisted together to give the necessary tension.

(a)



(b)



Fig. 114. Mr. F. T. Moore's case

(a) Patient with collapse of nasal framework.
(b) After reconstruction including a post-nasal inlay.

PATHOLOGICAL LESIONS RELATED TO PLASTIC SURGERY

There are a number of pathological lesions of the skin which are of special importance and relevance to plastic surgery. These include lupus vulgaris, congenital and tertiary syphilis, keloid formation, radiation necrosis, certain tumours involving the skin (such as melanoma and hæmangioma), and malignant disease of the skin.

Beyond the special regional problems which have been considered in a previous chapter, these conditions are of sufficient importance to justify separate consideration in terms of surgical pathology and treatment.



FIG. 113. Patient with gross ectropion of eyelids due to lupus vulgaris of 60 years' duration

LUPUS

Patients with lupus vulgaris in the untreated phase should never be submitted to surgery. But treatment by a competent physician using modern therapy is likely to make surgical intervention possible in due course for extensive and destructive lesions. The two areas for which reconstructive surgery is most commonly needed are the nose and the eyelids. The difficulties of nasal repair are often aggravated by adjacent scarring of cheeks and forehead; for this reason it may be impossible to find local tissue to provide lining flaps. In extreme cases the nose can be reconstructed only by using a thoraco-acromial tubed pedicle, the lower end of which is turned in to constitute a lining.

Eyelid repair may be needed in patients with longstanding lupus of the cheek (Fig. 113). Chronic scarring produces contractures which cause gross ectropion of the lower eyelid. The proper remedy is to introduce new skin on a generous scale after fully establishing the defect at the start of the operation. A split skin graft applied on a mould is the best method.

SYPHILIS

The mutilating effects of congenital or tertiary syphilis are well known, though fortunately less commonly seen in recent years. The nasal lesion is usually the most conspicuous and humiliating for the patient, and it must be emphasized that the gummatous process readily attacks both cartilage and mucosa. The repair of the resultant

factor may be keratin, derived from the buried roots of languo hairs or from sebaceous glands. There is a considerable weight of clinical, histological, and experimental evidence to support this hypothesis.

The treatment of keloid is best considered primarily in terms of prevention. All operative incisions must be carefully planned to follow the lines of skin tension, as shown by the direction of the skin folds and the pattern of the fine hairs. If it is necessary to cross the skin folds, say vertically at the wrist, the incision must be staggered in the form of a U or a Z. Elective operations on the young, if not urgent, may well be postponed until after puberty, particularly if either the systemic or local omens are poor.

The management of established scars which show hypertrophy depends on a wise combination of excision (or readjustment by a Z-plasty) with radiotherapy before and after operation. The work of Levitt, using a low kilo-voltage at a short distance, has shown how much can be accomplished. The rationale of radiotherapy is mainly related to a reduction of vascularity. This effect, together with an inhibition of early proliferation of the epidermis, may be used prophylactically for scars which are thought likely to become hypertrophic.

It should be added that even favourably placed facial scars due to injury are liable to remain indurated for several weeks, and the operation of excision and secondary suture should be postponed, if possible, for as long as 4 months.

RADIATION NECROSIS

The admirable results which accrue from proper radiotherapy are seen in almost every field of surgery. There are, unhappily, occasional examples where irradiation has been used for relatively trivial conditions in grossly excessive dosage. These cases are now much rarer than in the past, when serious X-ray burns were not infrequent. These burns were apt to be seen in relation to such non-malignant conditions as psoriasis of the hands, plantar warts or pruritus ani. In contrast, the correct and proper irradiation of a malignant growth may occasionally produce an area of skin necrosis which also requires surgical treatment.

The excision of any ulcer or area of severe radiodermatitis is a matter of importance on account of the risk of malignant change, a basal cell carcinoma being the most frequent complication of this kind.

Skin reconstruction should be planned and carried out at the same time as the excision. On account of endarteritis of the vessels in the deeper tissues, a free skin graft is seldom justified, and some type of skin flap is indicated. In the perianal region large rotation flaps are useful, while for the hands or feet a direct abdominal flap or cross-leg flap may be necessary.

PIGMENTED TUMOURS

The common "mole" of the face is so universal that it is subjected to every kind of mal-treatment. Fortunately malignancy is a very rare complication and the primary malignant melanoma is not often seen on the face outside the orbit. If the removal of small "moles" is indicated on social grounds, the excision should be in the form of an ellipse, with direct closure by sliding flaps.

Larger pigmented tumours may require excision with a free graft. The hairy variety are so uniformly benign that serial excision in two or more stages has been practised.

skin flap—is frequently insufficient, though in less severe cases it may produce adequate improvement.

Two alternative procedures must be considered. Joseph's three stage repair depends on first establishing the defect by boldly cutting across all layers transversely; skin is then sutured to mucosa. In due course a second operation is carried out; local skin flaps are turned in to provide lining and a forehead flap is attached as cover. Finally the flap is divided and its base is returned to the forehead.

The other plan depends on establishing a large defect behind the nasal skin, which is separated by dissection from the collapsed framework; this large space is lined by a post-nasal epithelial inlay and supported by a concealed prosthesis which is usually an extension of the upper denture (Fig. 114). This should give a reasonable profile, but it is troublesome both for the surgeon to execute, and for the patient to maintain in a proper state of hygiene.

KELOID

A true keloid is a progressive condition in a scar, associated with excessive bulk, increased vascularity, and abnormal induration. The lesion looks red and shiny and the patient usually complains of irritation. This relatively rare condition must be distinguished from the simple scar hypertrophy that is commonly seen, but which tends ultimately to regress leaving a wide papyraceous scar. In their early phase both lesions present a similar clinical and histological appearance, though time will ultimately establish the differential diagnosis.

In the case of a true keloid, the surgeon should adopt a very wary attitude. Simple excision of the scar will almost certainly lead to a still more disfiguring lesion. Excision, accompanied by radiotherapy or in special circumstances by cortisone therapy, is a possibility; but the patient cannot be assured of success. It may, in fact, be best for the lesion to be treated by radiotherapy alone, without adding any surgical trauma.

On the other hand hypertrophic scars, to which the term "keloid" is so frequently misapplied, are a less intractable problem; but some knowledge of their nature and ætiology is desirable. Hypertrophic scars are more liable to occur in certain patients; negroes, "redheads," and patients with thick greasy skins are said to be types who should be suspect. Frequently, however, the surgeon's fears prove false and all ends well. The most definite indication of an undue tendency to produce hypertrophic scars is the clear history that such a thing occurred on a previous occasion. Even then the patient's subsequent performance may show a great improvement. In general it is probably true to say that (excluding infants) the hazards of scar hypertrophy diminish as the patient grows older.

Local factors are of considerable significance. Scars which cross the normal lines of tension, especially when they also cross a concavity, are likely to become hypertrophic. Vertical scars across the antecubital fossa or below the chin are obvious examples. Local infection—even when of brief duration—favours keloid formation, and this is particularly evident if the infection is due to retained dirt or other foreign matter. Apart from infection, nearly all foreign bodies have a local irritative effect and their origin may be exogenous or endogenous. They include grains of dirt or fragments of dressings. It has been noted that the presence of fine languo hairs, often seen in children, is associated with scar hypertrophy. Mowlem and Glucksmann have suggested that the main endogenous

The incidence of involution is related to the depth of the tumour, since a number of strawberry nævi are not wholly superficial. Wallace, in a 7 year follow-up review, found that involution failed to occur in only 3 out of 290 superficial nævi, and in 8 out of 121 cavernous nævi. Involution mostly occurs during the first 4 years of life.

Having established the *probability of involution*, we must consider how to assess and treat these patients. A strawberry nævus which appears static at 6–12 months, which is not tending to bleed or ulcerate, and which is causing no functional embarrassment, should be observed and not submitted to irradiation, heat, or surgery. In borderline cases the appearance of grey flecks on the surface of the lesion is a favourable sign of incipient regression.

Nævi which show any signs of continued growth after 1 year, or have reached alarming proportions, then or earlier, must be considered in terms of radical surgery. Ulceration or hæmorrhage are hazards which should be prevented in good time, and the possibility of these complications is an indication for intervention.

Cavernous Hæmangioma

It is not possible to differentiate with precision between cavernous hæmangiomata and certain of the examples already described. The important distinction is between superficial and deep lesions, and it has already been said that some "capillary" nævi show both superficial and deep elements.



FIG. 115. Mr P. H. Jayes' case.
Infant with cavernous hæmangioma showing ulceration. This lesion has since been treated expectantly with rapid involution, and ultimate disappearance of the tumour.

Hæmangiomata which are predominantly cavernous are a serious menace (Fig. 115). Though spontaneous regression of the smaller lesions may occur, treatment should usually be carried out at an early stage. Careful coagulation by diathermy is often the best method, though there are keen advocates of sclerosing fluids such as 33 per cent saline or even boiling water. It may be possible, where the cheek or lip is involved, to pass a diathermy needle through the lining mucosa and into the angioma. In this way coagulation can be obtained without burning the skin. In any case repeated punctures using a moderate current, possibly at several separate sessions, are better than a more reckless approach.

In the large and dangerous varieties of cavernous hæmangioma, radical excision is required. Preliminary sclerosis or diathermy may however assist in carrying out the operation, or may justify a temporary postponement of surgery on a young child.

Arterial Hæmangioma

A pulsating hæmangioma must be regarded as arterial. The vascular anastomosis is usually so free that a preliminary ligation is of no advantage, and may even extend the

Any pigmented lesion which is growing, or which tends to bleed, or whose margin is indefinite, must be regarded with suspicion. In such cases the only safe method of biopsy is a wide primary excision. If the tumour involves the eyelids, exenteration of the orbit will, as a rule, be fully justified.

The sole of the foot is a notoriously dangerous site. A wide local excision with an immediate free graft is necessary, and most surgeons favour a block dissection of the inguinal lymph glands even when there is no direct evidence of invasion.

HÆMANGIOMA

The classification, natural history, and treatment of hæmangiomata have long been matters of controversy; but there has lately been considerable clarification of these questions, and it should now be possible to review the problem and submit definite answers.

The classification suggested by Matthews is comprehensive and logical, the following being a simplified version.

Spider Nævus

This is usually an isolated lesion, often seen near the nose or eyes. It consists of a central "vein" with tiny radiating vessels. It often disappears in early life, but if still present at the age of 10 it may need treatment for cosmetic reasons. Under local anæsthesia a fine diathermy needle is inserted into the central vessel. A momentary passage of current should give a permanent cure, though additional diathermy may be needed for the subsidary venules. In this, and all comparable conditions, diathermy should be used with delicacy and restraint.

Capillary Hæmangioma (Superficial)

These are of two main types: (1) Nævus Flammeus (port-wine stain); (2) Strawberry Nævus.

The nævus flammeus is a superficial capillary lesion, and regression cannot be expected. Vascular nodules may tend to develop as the patient reaches adult life, and these will increase the disfigurement and the risk of hæmorrhage. Both diathermy and irradiation (usually by thorium-X) have been advocated, but in the writer's view are seldom justified. Special cosmetic "cover creams" are often the best remedy available, more especially for large smooth lesions in awkward positions; nodular excrescences however may constitute a strong reason for surgical intervention. A localized lesion may be excised and the defect closed by local flaps. A large lesion presents formidable problems. If surgery is warranted, excision and grafting must be carried out in stages, with careful planning to avoid serious contractures and ill-placed scars.

The strawberry nævus is a much less static lesion. It usually appears a few days after birth and at first grows fairly quickly. It is raised and bright red, with a slightly irregular surface.

The crucial issue concerns the chances of involution. It must be stated categorically that *the majority of these tumours do undergo either complete or partial involution.* The fact that they are so rarely seen in adults (except in a much modified guise) is incontrovertible proof of this assertion.

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lesion. The tumour must be "circumcised," with ligation of the numerous entering vessels, and it can then be removed as a single procedure. In competent hands this is seldom a dangerous operation; but occasionally perforating vessels are found entering from adjacent bone, and hæmostasis may then be a truly desperate task.

CARCINOMA OF THE SKIN

The face is the chief site for *basal cell carcinomata* but by no means the only one. Although metastasis is virtually unknown, these tumours are potentially a great menace to life as well as health. The typical "textbook" appearance—a tiny lesion with rolled edges, so often casually labelled "rodent ulcer"—is important as an aid to early recognition and prompt treatment (Fig. 116). But many of these tumours are far from typical, and show a strong tendency either to infiltrate the adjacent skin, with very little outward evidence of their extent, or to burrow deeply into the underlying tissues.



Fig. 116 Early carcinoma of skin

These tendencies have an important bearing on the proper extent of the excision when early surgery is carried out. Both in area and depth it is imperative to remove a margin of uninvaded tissue. The sites in which these tumours most frequently occur are apt to complicate the technical problems of removal, even when the growth is small and localized. Particularly at the inner canthus, and along the margin of the lower eyelid, excision must not be influenced by the difficulty of the repair, nor even by considerations of sparing the patient a possible disfigurement. Skilful reconstruction will go a long way towards mitigating these ill-effects; for the ideal at which the plastic surgeon aims is to be competent to repair any defect which the exigencies of the operation create. And it must never be forgotten that the mutilations of unarrested basal cell growths are among the most terrible known to pathology.

It is often impossible to distinguish, by clinical appearance, between *epithelioma* and basal cell carcinoma of the face. Epithelioma is notably prone to occur on the lips and in the mouth, but its treatment in these sites is outside the scope of this chapter. It is only necessary to stress that any doubtful lesion of this kind must be assumed to be squamous cell cancer until there is histological proof to the contrary.

Treatment. *The local treatment* of malignant disease of the face immediately raises the question of radiotherapy versus surgery. There can be no dispute as to the impressive results of irradiation in expert hands for selected cases. Recent work confirms that the 5 year cure rate of non-infiltrating basal cell tumours by radium or X-rays is between 90 per cent and 95 per cent. Nevertheless, many authorities believe that, with few

exceptions, all basal cell tumours should be treated by primary excision, whatever the site. Wakeley and Childs stress the difficulties in assessing radio-sensitivity and claim that there should be "no recurrence with adequate surgical excision." "Adequate" is clearly the significant word, and carries important implications for the surgeon.

There is general agreement that for recurrences following unsuccessful irradiation, radical surgery is the best, and indeed the only proper treatment.

The criteria of adequate surgical treatment are clear: to excise the growth with a sufficient margin of normal tissue around and below the tumour; to repair the defect in a manner which will neither delay the recognition of recurrence nor leave an unnecessary deformity; and to deal adequately with any channels of lymphatic drainage which may be implicated.

While definitive primary repair has obvious advantages, it may be necessary in certain circumstances to leave a modified defect for an interim period. This is eventually repaired as a secondary procedure after a suitable delay, when there is no evidence of recurrence or infection. However, the increased scope of skin flaps (particularly from the forehead) has made it possible in many cases where there is a fistulous opening into the nose or antrum, or exposed bone without periosteum, to close these defects at the primary operation. On the other hand a split skin graft may be the best means of repair provided the raw area has an adequate blood supply, and in the presence of a thin graft any recurrence is more quickly evident; this is particularly true at the inner canthus of the eye.



FIG. 117 Late basal cell carcinoma with destruction of orbit, nose, and ethmoids

Secondary repair is indicated in those cases where the growth has been successfully eliminated by radiotherapy or surgery, leaving a residual defect. This frequently involves a fistula or sinus; there may be a small opening into the nose or frontal sinus; or the patient may have gross destruction of a large part of the face, with antrum, ethmoids, and orbit laid open (Fig. 117). It is seldom impossible to treat these deformities, and repair (in spite of grave cosmetic limitations) is usually desired by the patient. In dealing with the larger defects, it is often necessary to turn local skin flaps inwards as lining These flaps are elevated and, hinging on the margin of the defect, are turned through 180 degrees so that they lie raw side outwards. Immediate cover is provided by a direct skin flap from the forehead or neck; or by a transferred flap which has been prepared in advance.

Camouflage by an external prosthetic appliance is best used as an adjunct to limited surgical reconstruction, there are, however, cases in which any reconstructive surgery is out of the question, and a prosthesis may be the only available measure of concealment. For such patients this is an invaluable boon.

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CHAPTER IV

PLASTIC SURGERY OF THE HAND

F. T. Moore

INTRODUCTION AND GENERAL PRINCIPLES

The human hand is a perfect piece of mechanism and we are all constantly dependent upon it. Approximately a third of all industrial accidents involve the hands. Most of these patients with hand injuries receive their hospital treatment from relatively inexperienced and junior members of the staff. A clear conception of the principles of treatment will do much to improve this neglected branch of surgery.

The operative repair of hand lesions involves a detailed knowledge of normal anatomy. It is not enough to rely on the dim memory of anatomy learnt many years ago. The hand surgeon must have a detailed knowledge of the excursions of tendons during movement, their size, shape, and synovial reflections.

The relations and function of the intrinsic muscles and in particular their relation to the extensor hood mechanism are details which the young surgeon does not always appreciate. It is only such detailed knowledge that prevents the anastomosis of tendons to nerves or removal of nerves in mistake for strands of fascia. The intimate association of nerves, tendons, and their sheaths, blood vessels, and fascial planes renders them liable to multiple injury at the same time. If the normal anatomy is not known it is quite impossible to recognize the lesion with even the least chance of affecting the best repair.

Accurate brief notes with graphic notations of the findings are essential. It is important that the site of injury is clearly recorded as RIGHT or LEFT, and whether the patient is right or left handed, and that the digits are referred to as the thumb, index, long (or middle), ring, and little fingers. The nature and manner of injury, and an exact account of the early treatment should be recorded. There are many factors which must be considered if the individual requirements of each patient are to be satisfied. The age of the patient, his work and leisure and their significance should be considered, for the problems of a labourer are different from those of a watch maker. Whilst the reconstructed hand may satisfy the patient in relation to his daily work, the fact, for example, that he is unable to continue his golf, may seriously influence his opinion of the result. It is useful to assess the patient's intelligence and his attitude to the injury. The possibility of compensation must be recorded because in some patients progress ceases until the legal responsibility for injury is finally established.

It is advisable to compare both hands. Differences of skin colour, texture, and temperature often become apparent. Tests for sensation may be misleading. For example, light touch tested by a wisp of cotton wool is often unappreciated by the calloused hand of the labourer. Stroking a digit with an examining finger or pencil causes slight movement of joints which the patient may interpret as touch. The variations in the peripheral distribution of the median and ulnar nerves often makes diagnosis more

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Split Skin Grafts. Thick free skin grafts cut with a razor knife, or a "dermatome" are extensively used to repair defects of the extensor surface of the hand. The raw area must have an acceptable base on which it can live. Bare bone, joints, tendons, and nerves

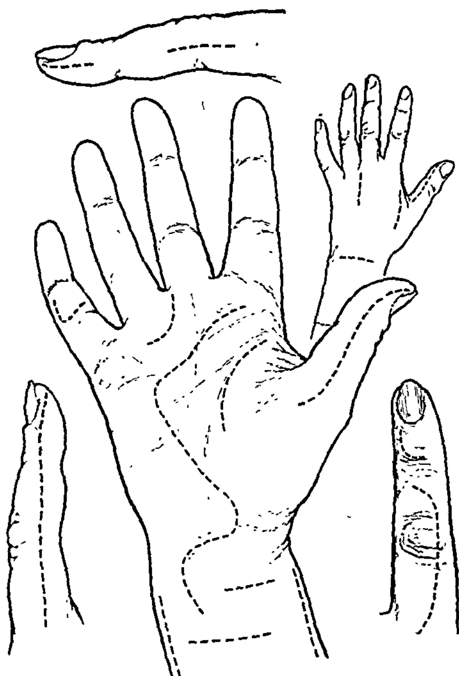


FIG. 118 (*a*) Diagram to show the type of incision which gives a *good* exposure, and does not cause disability They are easily extended.

are unsuitable beds, and alternative methods of grafting should be used. The base must be surgically clean and hæmostasis must be perfect. The split skin graft must be maintained undisturbed in contact with its base by means of a pressure dressing. Lastly, great care must be taken to ensure that the "shape" of a free graft does not produce limitation of function by contraction of badly sited marginal scars. For example, if the free graft is to

difficult. Sometimes the disability in the hand is due to pathological conditions elsewhere, such as poliomyelitis, syringomyelia, or a muscular dystrophy, while displaced cervical discs or a scalenus anticus syndrome can be misleading if one does not consider them. Serious omissions are avoided by detailed examination. If the injury or lesion has been a long standing one, involving enforced idleness and perhaps discomfort or pain, the examiner may feel he is dealing with a malingerer. Undoubted loss of use of a hand or hands often induces very disturbing psychopathic changes in personality. For example, a highly trained radar mechanic who is compelled to earn a living at a job he dislikes, as a result of injury to a hand, may require supportive psychotherapy to cure him of a very real hand disability.

It is impossible to dissect among the closely packed tendons and nerves in a field obscured by blood. Operative procedures on the hands must be carried out in a bloodless field obtained by a pneumatic type of tourniquet, the usual maximum pressure being 280 mm. As a rule ischæmia produced by a tourniquet should not be maintained longer than 1½ hours, and if a longer period of operating time is required the tourniquet should be released for 5–10 minutes every hour. It has been argued that the ischæmia produced by tourniquets may tend to induce a generalized tissue reaction, with delayed healing and prolonged residual stiffness in a previously mobile hand. But the advantages of a bloodless field far outweigh these objections which are largely theoretical.

PROBLEMS OF SKIN COVER

INCISIONS

An incision in the hand must be placed to afford the maximum exposure without damage to the tendons, nerves, and blood vessels, and must leave no residual disability. Most incisions are made in the natural creases of the palm and on the mid-lateral surfaces of the fingers. A median longitudinal incision which crosses flexion creases in the finger and palm is a surgical error whose ill-effects will become increasingly obvious as the scar slowly contracts pulling the finger down into flexion. It is equally important that incisions should *not* be continuous from the palm into the fingers, except a mid-lateral incision along the radial border of the index finger and ulnar border of the little finger. Incisions or extensions of existing wounds in the palm should be transverse or oblique, and so placed that they do not overlie freely gliding tendons. To find the best method of extending wounds due to trauma, to gain proper exposure for tendons or nerve repair, is often a difficult problem. The diagrams (Fig. 118 (*a*), (*b*)) indicate the type of incision which gives good exposure without causing a disability.

It is a cardinal rule of hand surgery that secondary healing by granulation tissue is never permitted. Whether the raw area is a result of trauma or a planned surgical operation, the wound must be closed since preservation of function depends so intimately upon intact skin cover. The fibrosis that accompanies the healing of raw areas by granulation involves the deeper structures to a greater or lesser degree. The scar will subsequently contract and will require a major surgical procedure to correct the deformity. Infected granulation tissue will convert a superficial lesion into a deeper lesion which may involve tendons, joints, muscles and finally nerves and blood vessels. Many methods are available for the repair of skin and subcutaneous tissue defects, the site and extent determining which method is selected.

of those more widely used in the hand described below will give some idea of their scope.

(1) The dorsal skin of a finger may be used to cover a defect on the volar surface but volar skin is *never* used for a dorsal lesion. Much depends on the shape and location of the defect. Sometimes it is possible to rotate the dorsal skin of the same finger into the defect. Other defects are dealt with by a cross-finger flap, in which a flap of the dorsal skin of an adjacent finger is attached to a volar defect. The cross-finger flap is particularly useful to cover a traumatic loss of a finger tip. Some surgeons prefer to raise a small flap on the thenar eminence to the finger, but as a general rule it is unwise to utilize the intact volar surface of the palm. These small flaps are detached on the seventh or tenth day and secondary defects are closed with split skin graft.

(2) Defects on the dorsum of the hand, if not too large, are easily closed by using adjacent skin as flaps.

(3) Sometimes it is possible to reconstruct the thumb web from the dorsal skin of the hand.

To close larger defects, skin must be brought to the hand from other regions. No hard and fast rule can be laid down by which method this is achieved but the following criteria are important.

(1) Any flap raised must be big enough. The commonest error is to make the flap too small.

(2) The thinnest skin produces the best skin cover for the hand.

(3) There should be a minimum raw surface between the attachment and base of the flap. Raw areas must be avoided by grafting all donor sites.

(4) The function of the hand must be maintained during the period that the flap remains attached.

(5) It is unwise to perform operations on joints or tendons during the stages of attachment of a flap.

Flaps are designed on the opposite forearm (cross-arm flap), from the acromiothoracic region, the abdomen, hypochondrium and rarely from the thigh. They are used to provide skin cover for the volar or dorsal surface. A method of attachment of the flap which persists from textbook to textbook and which I must condemn is the so-called "pocket or glove flap," in which a tunnel under the skin is prepared in the abdominal wall into which the hand is inserted. The disadvantages are obvious, the chief being the difficulty in keeping the wound clean.

All these procedures are in the province of the expert and are inappropriate for the novice "trying his hand" for the first time. It is not good enough to succeed in transferring a flap to the hand with the wrong choice of skin, the several operations taking several weeks, and the end result being a "poached egg" sitting in the middle of dense scar. Rank sums up the problem in relation to injuries to the finger tips as follows: "A carpenter with a shortened finger who can return to his work is better off than one with a valuable flap which prevents him doing his job without unreasonable details of care and constant awareness of his defect. Management must be planned in relation to practical value and not surgical fantasies."

The fillet flap should be mentioned. In some injuries in which two or more fingers are seriously damaged, defects in skin cover can be overcome by filleting a damaged finger and using the intact skin obtained as a flap to an adjacent finger.

be permanent, the shape of the recipient site must be prepared so that scars on the fingers are mid-lateral or transverse, and that webs are tailored so that "surgical syndactaly" does not occur.

Very thin split skin grafts are used as temporary skin dressing only when their subsequent replacement is envisaged. Full thickness Wolfe grafts are best suited to

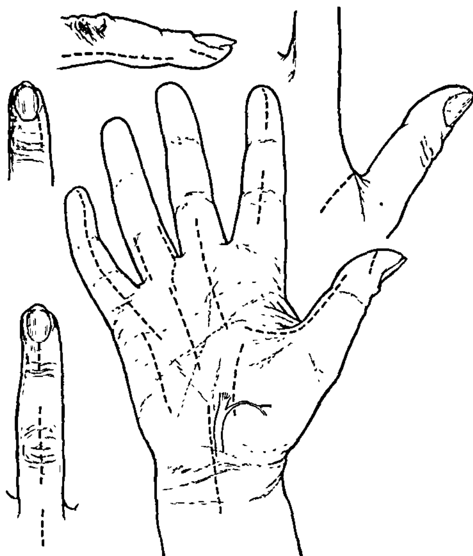


FIG 118 (*b*) This diagram illustrates incisions which are condemned because they cross flexion creases, may divide nerves, and are situated on tactile surfaces.

defects on the volar surface. Although they do not take as readily as thinner grafts they are relatively free from contraction and give a less rigid and more permanent cover. Particular care must be exercised regarding the shape of the recipient area so that suture lines do not cross flexion creases at right angles.

Local Flaps. Local flaps should be used whenever possible for skin defects. Such a flap can be used only for small defects and where the secondary defect can be adequately covered by a split skin graft. Flaps have the advantage that they carry subcutaneous tissue and produce a harder wearing skin to which sensation rapidly returns. There are large numbers of local flaps which only experience can teach the surgeon to use, but a few

of those more widely used in the hand described below will give some idea of their scope.

(1) The dorsal skin of a finger may be used to cover a defect on the volar surface but volar skin is *never* used for a dorsal lesion. Much depends on the shape and location of the defect. Sometimes it is possible to rotate the dorsal skin of the same finger into the defect. Other defects are dealt with by a cross-finger flap, in which a flap of the dorsal skin of an adjacent finger is attached to a volar defect. The cross-finger flap is particularly useful to cover a traumatic loss of a finger tip. Some surgeons prefer to raise a small flap on the thenar eminence to the finger, but as a general rule it is unwise to utilize the intact volar surface of the palm. These small flaps are detached on the seventh or tenth day and secondary defects are closed with split skin graft.

(2) Defects on the dorsum of the hand, if not too large, are easily closed by using adjacent skin as flaps.

(3) Sometimes it is possible to reconstruct the thumb web from the dorsal skin of the hand.

To close larger defects, skin must be brought to the hand from other regions. No hard and fast rule can be laid down by which method this is achieved but the following criteria are important.

(1) Any flap raised must be big enough. The commonest error is to make the flap too small.

(2) The thinnest skin produces the best skin cover for the hand.

(3) There should be a minimum raw surface between the attachment and base of the flap. Raw areas must be avoided by grafting all donor sites.

(4) The function of the hand must be maintained during the period that the flap remains attached.

(5) It is unwise to perform operations on joints or tendons during the stages of attachment of a flap.

Flaps are designed on the opposite forearm (cross-arm flap), from the acromiothoracic region, the abdomen, hypochondrium and rarely from the thigh. They are used to provide skin cover for the volar or dorsal surface. A method of attachment of the flap which persists from textbook to textbook and which I must condemn is the so-called "pocket or glove flap," in which a tunnel under the skin is prepared in the abdominal wall into which the hand is inserted. The disadvantages are obvious, the chief being the difficulty in keeping the wound clean.

All these procedures are in the province of the expert and are inappropriate for the novice "trying his hand" for the first time. It is not good enough to succeed in transferring a flap to the hand with the wrong choice of skin, the several operations taking several weeks, and the end result being a "poached egg" sitting in the middle of dense scar. Rank sums up the problem in relation to injuries to the finger tips as follows: "A carpenter with a shortened finger who can return to his work is better off than one with a valuable flap which prevents him doing his job without unreasonable details of care and constant awareness of his defect. Management must be planned in relation to practical value and not surgical fantasies."

The fillet flap should be mentioned. In some injuries in which two or more fingers are seriously damaged, defects in skin cover can be overcome by filleting a damaged finger and using the intact skin obtained as a flap to an adjacent finger.

THE HEALED BURNED HAND

The repair of a healed burned hand resolves itself into two problems: skin replacement of scar by grafts and mobilization of joints and tendon. Skin replacement is indicated whenever function is restricted by keloid, or the contracture of scarred skin. This contracts equally in all directions, sometimes pulling the hand into bizarre positions. *Burns on the dorsal surface of the hand are easier to treat than burns on the palmar* surface, because split skin grafts on a concave surface tend to contract, and the power of the extensor muscles is insufficient to prevent it. On the other hand the more powerful flexor muscles are able to maintain constant traction on a graft on the dorsal surface until the contractile phase of the graft is over.

Dorsal Burns. Full thickness burns of the dorsum may involve the extensor tendons and the extensor mechanism in varying degree. The most vulnerable site is over the proximal interphalangeal joints where the extensor mechanism is thin; even if this has not been damaged by burning, it may soften and disintegrate as a pannus of granulation grows over it. The damage is irreparable because the underlying joints become injected. The unopposed pull of the flexor tendons drag the finger into flexion at the proximal interphalangeal joint and the lumbrical and interossei muscles pull the terminal joint into hyperextension. The dorsal scar may contract, reversing the normal metacarpal arch and gradually pulling the fingers into hyperextension at the metacarpophalangeal joints. Flexion becomes impossible and the collateral ligaments shorter through disuse, causing further disablement. The lumbrical and interossei muscles will then act as extensors of the metacarpophalangeal joints. The hand becomes a useless claw and surgical correction is a most difficult problem.

TREATMENT

The dorsal scar is outlined with surgical ink, thus defining the area to be excised. Small indentations are made at the level of joints so that as the contracting suture line is "staggered" and interference with function is prevented. Retraction of the extensor hood mechanism in a distal direction will reveal the contracted collateral ligaments of the metacarpophalangeal joints and these are excised. It is then possible to flex the fingers at the metacarpophalangeal joints. A thick split skin graft cut with a dermatome is then tailored into the skin defect, taking care to establish the webs between the fingers and the thumb The hand is immobilized in the position of function for 7–14 days before the first dressing is carried out. Intense active exercises are then begun depending on the condition of the graft, etc. After an interval of 2–3 months the proximal interphalangeal joints are, if necessary, arthrodesed in a position which takes into consideration the patient's work and hobbies (Fig. 119 (*a*), (*b*), (*c*), (*d*)).

Rarely a dorsal burn may destroy the extensor tendons and damage the underlying bone. *A split skin graft rarely gives a satisfactory result in such a deep burn. If* it is intended to attempt reconstruction of the damaged tendons a skin flap with subcutaneous tissue is employed. A direct abdominal flap or a tubed pedicle (graft) raised from the skin of the abdomen is often used.

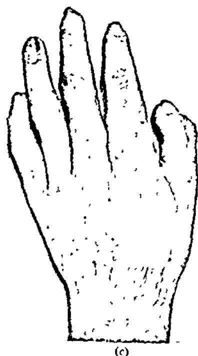
Palmar Burns. Healed burns of the palmar skin are very prone to contract dragging the fingers into flexion and the thumb towards the palm. The scar must be excised and this may consist of the entire surface skin of the palm and volar surface of the digits.



(a)



(b)



(c)



(d)

FIG 119 (a), (b) Hyperextension deformity following a deep dorsal burn.
(c), (d) Excision of dorsal scar and replacement by a thick split skin graft combined with excision of the metacarpophalangeal collateral ligaments gives a good working hand

Great care must be taken to ensure that all incisions are so placed that contraction of suture lines will not interfere with function. A thick split skin graft cut with a dermatome is used to replace the contracted scar. These split skin grafts contract more than thick grafts and are not used for this reason. Hæmostasis must be absolute.

DUPUYTREN'S CONTRACTURE

Incidence. Dupuytren's contracture occurs in approximately 1 per cent of the population. It is common in the fourth and fifth decade, but does not occur in the very young and very old. It affects males approximately six times more commonly than females. It is more prevalent in patients who do not use their hands for manual work than in manual workers, in the proportion of 55–45 per cent respectively (Bunnell).

Ætiology. It is hereditary in many cases. It has been claimed that gout, rheumatoid arthritis, and diabetes are often associated with Dupuytren's contracture. Skoog found that in 207 male epileptics 42 per cent had Dupuytren's contracture. The condition is bilateral in over 50 per cent cases and is occasionally associated with contracture of fascia elsewhere in the body. The commonest other site is a similar condition on the medial side of the plantar fascia of the foot. It has also been noted that contraction of the fascial planes separating the corpora cavernosum and spongiosium produces distortion of the penis (Peyronie's disease) which is sometimes associated with Dupuytren's contracture. There is definite evidence that trauma may be responsible for a few cases. Statistically there is a significant preponderance for right hand in unilateral cases. Nevertheless, the left hand is involved in many unilateral cases. Also the thumb and index are more used than the other fingers, but the disease is least common in these fingers. It is frequently bilateral although one hand received the most trauma. There are many injuries of the palm, but these are not followed by Dupuytren's contracture. Subcutaneous nodules on the dorsal aspect of the proximal interphalangeal joints (knuckle pads) are common.

Symptoms. Often a feeling of discomfort draws the patient's attention to a small area of thickening beneath the skin of the palm. It may remain so for many years but usually over a period of 1–2 years it spreads proximally and distally gradually contracting, firmly dragging the fingers involved into flexion. The ring finger is most frequently affected, then the little, long, index, and thumb in that order. The clinical severity of the disease can be divided into four groups.

(1) Involvement of the palmar fascia without contraction or skin involvement.

(2) Involvement of the palmar fascia with moderate flexion of the fingers and with skin involvement.

(3) Involvement of the palmar fascia with severe flexion of the fingers.

(4) Involvement of the palmar fascia, skin, and joints.

With increasing flexion of the fingers the volar skin becomes soggy, infected, and foul. The grip gradually weakens and many are unable to work.

Diagnosis presents no difficulties. It is sometimes confused with congenital flexion of the fingers which is maximal at the proximal interphalangeal joints. Injuries of the palm or of the volar aspect of the fingers followed by longitudinal scars may produce flexion deformities of the fingers. Flexion contractures may occur secondary to infection

of the palm or fingers. Prolonged immobilization in flexion causes shortening of joint capsules and ligaments. Volkmann's ischæmic contracture should be easily recognized as are the deformities produced by the rheumatic group of diseases.

Pathology. Dupuytren's (1832) description of a patient he treated is as follows: "Exposing the palmar fascia I was astonished to perceive that this fascia was tense, retracted, and shortened. From its lower portion were given off kinds of cords, which passed to the diseased fingers ... I cut through the prolongations extending from the fascia to the fingers; the state of contraction immediately ceased ... I examined the tendons with care. Their surfaces were smooth and they enjoyed their usual degree of motion; the joints also were in a healthy state."

Secondary changes occur in joints that are permanently flexed. Capsule and ligaments shorten, and the joint cartilages degenerate gradually, altering the shape of the joint surfaces. Gradually skin, nerves and blood vessels become secondarily contracted so that even after removal of the palmar fascia the finger cannot be straightened.

Histologically the essential feature of the disease is a "benign" fibroplasia of the palmar connective tissues (Horwitz, 1942). This author pointed out the striking resemblance to the other localized fibroplasias such as keloids and fascial dermoids. Clay (1944) on the other hand came to the conclusion that the disease was due to a neoplasm—a cellular fibroma of the palmar fascia.

Treatment. The whole of the affected portion of the palmar aponeurosis must be excised if a permanent cure is to be achieved. In this way both the primary cause of the deformity and a site for a relapse are eliminated. In patients with bilateral deformity the hand least affected should be treated first because a poor result on a badly crippled hand would make the patient disinclined to submit to further surgery.

The operation is performed under general anæsthesia. A bloodless field is attained with an Esmarch bandage and a pneumatic type of tourniquet; the Esmarch bandage is removed as soon as the tourniquet is inflated to approximately 260 mm. of mercury.

A transverse incision is made in the distal transverse palmar crease and the skin covering the palmar aponeurosis is undermined. In severe cases prominent contracted cords are divided transversely to permit extension of the flexed fingers. A careful dissection of every vestige of diseased palmar fascia is made. Nerves, particularly those to the lumbrical muscles, must be identified before severing tissue. Great care must be taken that tendon sheaths remain undamaged. Tight septa extending from palmar fascia to the deep fascia of the palm are excised. The tendons of the interossei muscles must not be mistaken for fibrous septa. Each affected finger is opened by a carefully planned Z-plastic incision. Experience and judgment are needed if the Z incision is to be correctly sited and designed. It gives an exposure unsurpassed by any other method. At the conclusion of the operation the transposed skin flaps increase the skin available in the long axis of the finger.

On completing dissection the tourniquet is released and hæmostasis secured. This may take twice as long as the dissection. The incisions are closed with very fine silk, nylon, or stainless steel wire leaving one or more tiny rubber drains in the palm. No attempt is made to straighten the fingers, because the devitalized skin will blanche and healing will be delayed. A generous "pressure" dressing is applied which permits free movement of the distal two finger joints. Drainage tubes are removed next day, and stitches on the tenth to fourteenth day. The duration of immobilization of the

metacarpophangeal joints will depend on the speed with which the palmar incisions heal. As soon as healing is complete active intense physiotherapy is begun. It is sometimes necessary to construct special splints to exert continuous traction through elastic bands to increase extension. A word of warning is needed: patients suffering from Dupuytren's contracture have a tendency to stiffness of the finger joints, and this may be aggravated by treatment, and prove a worse evil than the original contraction. An unrecognized hæmatoma or too tight a pressure dressing may precipitate a pathological process which

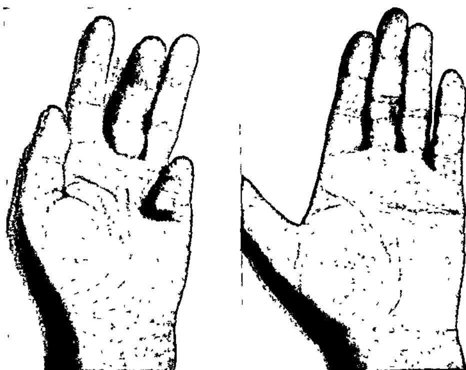


FIG 120 Photograph taken before aponeurectomy and 6 weeks later. The healed incision in the palm and the Z exposure in the fifth finger are visible

resembles Sudeck's atrophy. Such a result is a catastrophe, but with careful treatment should be avoided (Fig 120)

It is sometimes permissible to amputate a grossly flexed finger in which joint changes are apparent. No hard and fast rules can be made, but it is a useful manœuvre in the very old and in some manual labourers. The involved finger is filleted and the skin cover is tailored into the palm to make good any shortage of palmar skin.

Fasciotomy.

Fasciotomy is often condemned because the contracted fascia is not removed and it is claimed that damage to the digital nerves is a frequent occurrence. If the patient is *carefully selected these criticisms are not justified I reserve fasciotomy for the older* patient with prominent palpable cords in the palm which are pulling a finger or fingers into flexion.

Fasciotomy is performed as follows The palmar skin is undermined by the extension of a small incision on the radial or ulnar border of the hand. A small fasciotome is then

used to divide the fibrous bands. The digital nerves are safe because it is very difficult to cut them unless they are under tension.

The results are most impressive. In approximately 50 per cent of patients operated upon the pathological change in the palmar fascia appears to be arrested and in 30 per cent resolve. Fasciotomy is a simple operation and can be repeated; a particularly useful procedure for aged and infirm.

CONGENITAL DEFECTS

Almost all types of congenital defect may be hereditary, but it has not been decided whether the mode of transmission is a dominant or recessive one. It was at one time a popular belief that many of these deformities could be explained by abnormal uterine conditions, such as amniotic bands or coils of the umbilical cord causing abnormal furrows or even amputations. Bagg (1924) showed conclusively that such theories were untenable. Many dietetic experiments on animals by depriving them of an essential food have revealed a possible factor in the ætiology. Bagg, by exposing mice to successive exposure of X-rays produced a strain prone to develop deformities of the paws. It has also been observed that women who suffer from rubella during the first 4 months of pregnancy sometimes have children with various congenital anomalies.

These congenital deformities produce an unlimited variety of lesions and they are often associated with anomalies elsewhere in the body. In the hand these deformities may be classified into five main groups.

(1) Fusion of contiguous digits which may involve skin alone or all tissue within the digit, usually called syndactyly.

(2) Absence of part of the hand.

(3) Congenital "amputations" complete or partial, the latter comprising constriction rings of wrist or digits.

(4) Duplication of one or more components, commonly seen as supernumerary digits.

(5) Axial rotation of digits caused by defects in the bones or soft structures.

Treatment. Much can be done for these unfortunate patients. It is necessary in some types of deformity to begin surgical repair before the child reaches 3 years of age, especially if further growth will increase the deformity. Surgical correction is mainly related to function in most cases, but abnormal appearance may alone justify repair. Mainly, deformities are best left alone if function is satisfactory and cannot be improved by surgery.

Syndactyly is the commonest deformity in the hand. The digital webbing may be an extension of the normal web or involve fusion of nerves, blood vessels, and bone. Deformities involving skin only are repaired before the patient reaches school age, but the more complex deformities are normally repaired during the second year. In all cases of syndactyly there is a shortage of skin and it is useless to attempt repair using only the skin of the web. The proper technique is to establish the depth of the cleft and to design volar and dorsal flaps, triangular or horseshoe shaped, based proximally at the level of the metacarpophalangeal joints. These flaps are interdigitated and the denuded side of each finger is covered by a split skin graft, applied on previously moulded dental compound (Fig. 121).

Polydactylism is one of the commoner deformities, and tends to occur most frequently on the ulnar or radial borders of the hand. A careful study of the X-ray photographs, consideration of the functional and cosmetic standpoints will usually indicate that those digits that oppose each other are those that are retained. Before amputation of a supernumerary digit it is necessary to be certain that the remaining digit has a normal sensation and working tendons.

Congenital annular grooves are frequently seen on the fingers. The grooves are often shallow extending into the subcutaneous fat, or they may involve the deep fascia even

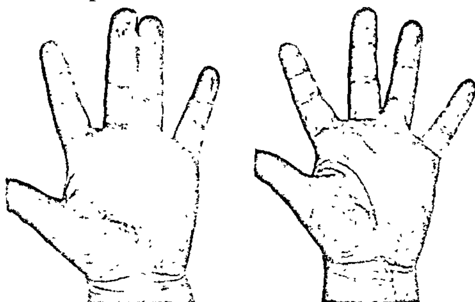


FIG 121 A case of syndactyly treated by the method described in the text

penetrating bone. The shallow rings so limit the nutrition of the finger that growth is arrested in utero and the finger is represented by a little bloob of skin.

Treatment consists of amputation of useless digits to improve the appearance of the hand and the so-called "pie-crust" operation to relieve œdema and improve the contour. The annular band is excised and then multiple triangular flaps are designed for interdigitation which will completely encircle the limb, giving a zigzag scar.

In the absence of digits, phalangization or deepening the cleft between the metacarpals may produce a good working hand. Sometimes the cleft is already too wide as in some lobster claw hands. It is possible to narrow such a cleft by moving digits towards each other, or removing the bone in the depths of the cleft to make the whole hand narrower. Other operations employed to increase function are tendon transplants, arthrodesis of joints, tendon lengthening, re-alignment of bones and excision of epiphyses to arrest growth. The adaptability of children to congenital defects is prodigious, and therefore great judgment is often required to decide when and by which method the best result will be obtained.

RECONSTRUCTION OF DIGITS

The loss of a thumb is a crippling hand injury equalled only by the loss of all fingers in a hand. The type of repair is determined by the presence or absence of a stump capable

of opposition. Opposition is a complex movement but it can be analysed into two main movements: flexion and rotation at the carpo-metacarpal joint, and secondly a pure flexor movement at the metacarpophalangeal joint. If an injury leaves intact the thenar group of muscles and a mobile carpo-metacarpal joint, operations aimed at lengthening the opposable remnants produce a good thumb. Loss of the whole thumb including the metacarpal bone is a more difficult problem and any operation that claims to restore opposition must fulfil the following conditions:

(1) Prehensile ability must be restored by apposition of the thumb and fingers, or movement of the fingers to the fixed thumb.

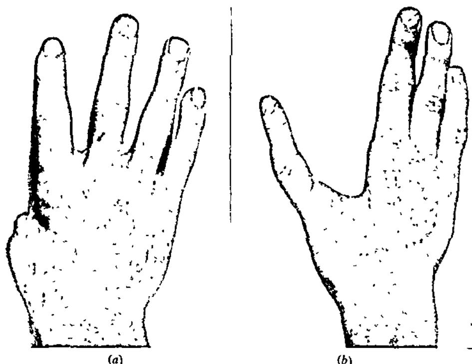


FIG 122 (*a*), (*b*) Before and after pollicization in which the full length of the index finger was used

(2) It must be strong enough to give an adequate grip.

(3) It must retain or restore adequate sensation in the new thumb.

Many methods are used to restore opposition—the following are the most widely used:

(1) Lengthening the short thumb by a peg bone graft and using local skin in the form of a "cocked hat" flap gives good results. It is impossible to secure a thumb of normal length but the reconstructed short thumb appears to possess almost at once some degree of tactile and thermal sensibility

(2) Transplanting an index finger to the position of the thumb (pollicization) fulfills most of the requirements for reconstruction of a thumb. A full length finger is often too long, but pollicization of an index finger shortened by the initial injury gives a thumb of good length.

(3) Phalangization or deepening the web between the thumb stump and index finger is often used when the remaining fingers have been shortened by the injury. Deepening

the cleft is of little value if the fingers are normal except when the thumb has been lost distal to the metacarpophalangeal joint.

(4) Rotation osteotomy of the index and little fingers will restore a pincer-like action to the hand. Osteotomies give better results when the long and ring fingers are also shortened by the injury.

(5) Lengthening of a thumb by a tubed pedicle graft, and stabilizing the skin graft on the base of the thumb by a bone graft, though widely used, is unsatisfactory as well as tedious.

A method has lately been developed by which part of the index finger with its nerve and blood supply can be transposed to the end of the thumb stump. A new thumb of almost normal length is obtained.

Loss of all fingers is difficult to treat. It is wise to wait for some weeks in order to find out exactly how much use is made of the hand. Much will depend on the patient's work and hobbies. Phalangization of the metacarpal bones does not give sufficient mobility to the stumps to justify the operation. Lengthening operations by bone grafts are doomed to failure unless the lengthened stump possesses normal sensation. Removal of the index and ring metacarpal bone using the excess skin to phalangize the remaining metacarpal bones gives better results (Fig. 122 (*a*), (*b*)).

CHAPTER V

ACTINOMYCOSIS OF THE FACE, NECK AND CHEST

ZACHARY COPE

THE actinomycetes form a group of micro-organisms slightly higher in the structural scale than the bacteria, but lower in complexity than the moulds. They grow by long, segmented, branching hyphæ, which sometimes form terminal spores. The large and closely allied family of the streptomycetes are somewhat similar, but their hyphæ have no cross-walls, and form no sporophores. Few of the actinomycetes are pathogenic to animals. The two most important pathogenic varieties are Actinomyces bovis and Actinomyces israeli (or wolff-israeli); the former affects cattle and the latter human beings. Until 1940 these two were thought to be identical, but Erikson and others have shown that there are slight differences between them. The culture of A. israeli has a firmer, rougher texture and is more adherent to the culture medium. The organism is more polymorphic and ferments sugars more than does the A. bovis. Both are anærobic, or more accurately microærophilic organisms.

There is also a large group of actinomycetes which are ærobic, are commonly found in nature, and are rarely pathogenic. They usually go under the name Nocardia. Some pathogenic varieties are well-known, e.g. A. eppinger, A. asteroides.

Actinomyces isræli is a delicate organism which grows slowly on special media, and does not resist drying. It is often difficult to obtain cultures from undoubted actinomycotic material. The organism has never yet been found outside an animal body.

Common Route of Entry

The most common route of entry is by the mouth. Since the organism soon dies when outside the body it is likely that it is transmitted indirectly by way of contaminated drinking vessels. The A. isræli has been found latent in the crevices of carious teeth or in the crypts of the tonsil of apparently normal persons. It does not cause a pathological lesion unless there is a break in the continuity of the lining epithelium permitting it to gain access to the deeper cellular tissues. The extraction of a tooth often forms a favourable opportunity, but abrasions of the mucous membrane by other means may provide the necessary opening. Half the cases of actinomycosis are to be found in the region of the face or neck. Another 20 per cent occur in the thorax. Here infection occurs either by aspiration of microscopic portions of the fungus into the air-passages or, possibly, by mediastinal infection following the escape of the organism through an abrasion of the œsophagus.

It is rare for the organism to gain lodgment in a lymphatic gland, but it is possible that the infection may be conveyed by the lymphatics, for occasionally the first detectable lesion is in the lower part of the neck.

Response of the Tissues

The reaction of the tissues is almost always subacute or chronic. If subacute a small

the cleft is of little value if the fingers are normal except when the thumb has been lost distal to the metacarpophalangeal joint.

(4) Rotation osteotomy of the index and little fingers will restore a pincer-like action to the hand. Osteotomies give better results when the long and ring fingers are also shortened by the injury.

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FIG 123 Actinomycosis of parotid region.



FIG. 124 Actinomycosis of parotid region (side view).

abscess may form in the upper part of the neck, and, unless the pus be examined microscopically, the cause of the condition may be overlooked. More commonly the side of the face gradually swells up and, if the soft parts alone are affected, a hard and often painless mass may distort the cheek. The mass is formed of hard fibrous tissue with foci of the fungus. Rarely both sides of the face may be affected. Within a month or two softening takes place either behind the angle of the jaw or near the inner canthus of the eye, and from the pus may be obtained the little "sulphur-yellow granules" of the fungus. The facial swelling then subsides, but only too often the infective process spreads gradually down the subcutaneous tissues of the neck and forms new abscesses lower down. Sinuses may form but no true ulceration occurs.

Sometimes the mandible is affected. This may take the form of a local osteitis near the dental focus from which the disease originated, or, more rarely, a cystic condition of the jaw may form. Occasionally the horizontal ramus may be much thickened and traversed by channels full of infective material. Periostitis is frequently seen.

In the days when there was no specific remedy for the disease the process occasionally spread upward to the pterygoid region and even entered the skull, usually with fatal results. The A. isræli may be present in the bronchial secretion without any untoward symptoms resulting. If it invades the tissues it may form a local abscess but more commonly it spreads gradually throughout the lung. An empyema commonly results, and frequently an abscess may point through one of the lower intercostal spaces. When the organism, escaping from the œsophagus, forms a lesion in the mediastinum, sooner or later an abscess will point posteriorly, lateral to the erector spinæ. A mediastinal focus of actinomycosis may affect the vertebral column, causing the formation of a certain amount of new bone but infiltrating and weakening the bodies of the vertebræ; rarely, collapse of a vertebral body may result.

Diagnosis of Actinomycosis

It is essential always to consider the possibility of actinomycosis in any subacute or *chronic lesion in the region of the face and neck, or in any chronic lung-lesion,* of doubtful causation. Whenever pus forms and escapes it should be carefully examined for the characteristic granules, and stained and examined microscopically for the mycelium (which is gram-positive). An attempt should be made to culture the organism anærobically.

In facial lesions an X-ray examination may show evidence of osteitis or periostitis. In thoracic lesions an X-ray of the chest may show a dark shadow indicating consolidation of that part of the lung involved—usually the lower part. In mediastinal lesions the shadow of the inflammatory mass may closely simulate enlarged lymph-glands or a mediastinal tumour. Pulmonary actinomycosis may simulate tuberculosis.

In a neglected case of cervico-facial actinomycosis the scarred and puckered skin of the neck with a discharging sinus or two, usually presents a pathognomonic picture. When dealing with an early facial lesion diagnosis is often in doubt until pus is obtained from a softened area.

Treatment of Actinomycosis

General. Extensive actinomycotic lesions cause a progressive anæmia and in such cases it is necessary to treat the general condition by methods similar to those adopted for



Fig. 123. Actinomycosis of parotid region.



Fig 124 Actinomycosis of parotid region (side view).

tuberculosis—complete rest, fresh air, sunlight (real or artificial), a nourishing diet, and hæmatinics such as iron. With severe anæmia such as occurs more often with visceral actinomycosis, a blood-transfusion may be needed.

Surgery

Incisions are sometimes needed to open abscesses or to drain an empyema. Excision of the affected part of the lung is now never required. When the mandible is greatly thickened and riddled with sinuses it may be necessary to remove some of the affected bone, leaving sufficient to maintain continuity.

X-ray Treatment

This is now seldom required. Occasionally it may be advisable to give some X-ray treatment to help in the softening of an indolent hard focus.

Drug Treatment

Most of the numerous drugs which were formerly recommended for actinomycosis have now been abandoned. Some benefit still accrues, however, from the administration of some form of iodine. Large doses of potassium iodide were formerly advised but are unnecessary. The simplest and best form to give is the tincture as recommended by Chitty, i.e. 5 minims of tincture of iodine given 3 times a day in a glass of milk. Fortunately the new therapeutic agents—the antibiotics and the sulphonamides—will cure most cases of actinomycosis. Penicillin is the most reliable therapeutic agent. Half a million to one million units daily is usually sufficient, but in obstinate cases up to two million units a day may be given. It is best to give two intramuscular injections within 24 hours; 3-hourly injections are very tedious for the patient. It is necessary to continue treatment for some time after all signs of the disease have disappeared; otherwise recurrence will be common.

If the strain of actinomyces proves to be insensitive to penicillin then recourse may be had to some of the other antibiotics—streptomycin (1 or 2 gm. daily), or aureomycin (2 gm. daily), taking all the precautions which are usual in such cases. Some of the newer antibiotics are also efficacious against the actinomyces, but the above should suffice.

The sulphonamides can sometimes be given with advantage. Sulphadiazine and sulphamezathine are recommended. For an adult an initial dose of 4 gm. followed by 1 gm. every 4 or 6 hours for 2 or 3 days. Here again the usual precautions should be taken. Sometimes better results are obtained by combining treatment by penicillin with the administration of one of the sulphonamides.

Prognosis

There are few cases of actinomycosis which cannot be cured, provided that the diagnosis be made reasonably early.

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CHAPTER VI

SURGERY IN THE TROPICS

STANLEY BELL

Introduction. While there are already established in the tropics certain centres with adequate staff, facilities, and equipment for extensive surgical treatment, and it is to be expected that the number of such centres will increase, most surgeons in tropical countries find that their resourcefulness and powers of improvisation are required to a greater degree than in the more developed parts of the world. Equipment, ancillary services, and nursing services may be deficient or lacking, and the surgeon may have to undertake responsibilities for his patients which in well-established centres he could delegate to other members of his staff.

THE SURGEON

In conditions of high atmospheric temperature and humidity the surgeon will find that he must reduce the length of his operating list. His clothing must be light and thin, but he must avoid sudden exposure to lower temperatures, for example between operations. With practice many operations can be accomplished while the surgeon is seated and this may prove a means of reducing fatigue. Care of the skin is most important where increased perspiration is a normal accompaniment of daily life. Occasionally in a person having an unrecognized or untreated tineal infection of the feet, a sensitivity state or dermatophytid reaction may occur, characterized by vesicular and scaling dermatitis on the fingers and hands. The surgeon who suffers from such a condition may be misled into supposing that his skin has become sensitive to one of the disinfectant lotions which he uses. The use of an antihistamine cream (Anthisan) on the hands, and the vigorous and persistent treatment of the tineal infection on the feet, for example with 5 per cent undecylenic acid ointment, will usually result in cure of the condition.

It is often the case that the surgeon in the tropics must operate without an assistant, and sometimes in addition must supervise the anæsthesia of the patient. These conditions may limit the length of the operating list. Furthermore allowance must be made for the fact that re-sterilization of instruments and other equipment may be slower than with modern sterilizing equipment in more developed centres.

THE THEATRE STAFF

In many hospitals in the tropics theatre assistants and nurses are incompletely trained. Their co-operation must be won and maintained by the attention which the surgeon pays to keeping their interest in the work which he is doing. Many such assistants prove invaluable because of their knowledge both of the local people and of their dialect, and by acting as liaison officers between the surgeon and the patient's relatives and friends. But their limited educational background must never be forgotten, for otherwise, in an emergency, the surgeon may be disappointed and annoyed because he expected too much of them. Great as is the value of a well-trained and experienced theatre sister in any surgical centre, it is far greater in centres where surgery is attempted in the tropics.

tuberculosis—complete rest, fresh air, sunlight (real or artificial), a nourishing diet, and hæmatinics such as iron. With severe anæmia such as occurs more often with visceral actinomycosis, a blood-transfusion may be needed.

Surgery

Incisions are sometimes needed to open abscesses or to drain an empyema. Excision of the affected part of the lung is now never required. When the mandible is greatly thickened and riddled with sinuses it may be necessary to remove some of the affected bone, leaving sufficient to maintain continuity.

X-ray Treatment

This is now seldom required. Occasionally it may be advisable to give some X-ray treatment to help in the softening of an indolent hard focus.

Drug Treatment

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The Patient

Some patients have sufficient education to realize the importance of symptoms and to give an adequate history, but many patients will be found to have little recollection of the timing and sequence of their symptoms. Consequently some doctors abandon hope of gaining any useful information from the patient's history and concentrate their attention upon physical examination. Patience and the use of the local dialect, or an efficient interpreter, will often prove rewarding.

The co-operation of the relatives of the patient should be sought. In many communities the individual is not expected to make important decisions for himself or herself, but relies upon the guidance of a group of friends or relatives. Needless to say their slowness in reaching a decision, and their desire to temporize may be most frustrating to the surgeon and sometimes dangerous for the patient. It is in these circumstances that the co-operative hospital orderly or senior nurse can be of the greatest help.

The religious or other beliefs of the local people must be taken into account in planning surgical treatment. For example, in many Muslim areas amputation will be refused and some form of conservative surgery will be all that is possible. Again in the case of proposed operative delivery of a pregnant woman the relatives will usually have little regard for the life of the unborn child but will be very concerned for the life of the woman.

Many primitive people are stoical in bearing pain but they fear the unknown. Therefore if the surgeon can bring his patient to regard the operation as only part of the treatment and can save him from anticipating unknown terrors he will frequently find that surgery is extra-ordinarily well tolerated by his patients.

Neglect of his condition, delay in seeking trained help, and time spent in trying various indigenous forms of treatment, often result in the patient appearing with very gross pathological changes or serious complications. It is to be recalled that multiple pathology is common in tropical areas. Apart from well-recognized differences in the incidence of some diseases related to the presence or absence of vectors of the causal agents there are some surprising and as yet little investigated differences in the local incidence of some conditions: for example, inguinal and umbilical herniæ, renal calculi, peptic ulceration, biliary disease, and some types of neoplasms.

Pre-operative Investigation and Preparation. Apart from those investigations which the surgeon considers necessary in the individual case, it is always wise to arrange examination of the patient's fæces, urine, and blood.

(*a*) Fæcal Examination. Usually naked-eye and microscopic examination suffices, but in some cases concentration techniques for protozoal cysts and helminth ova, cultural methods for bacteria, and certain chemical tests may be required. Parasitic worms in the intestine are common, and some of the more important of these are roundworms, hookworms, and tapeworms. Vegetative or cystic forms of protozoa may be found, of which the most important is *Entamœba histolytica*.

Roundworm Infection (*Ascaris Lumbricoides*)

These worms are common parasites especially in children. They may cause vague abdominal discomfort and colic, or the patient passes a worm in his stools, or a worm is regurgitated and vomited. Uncommonly, large numbers of these worms coiled together become impacted in the intestine and cause obstruction. Rarely adult worms migrate

into the appendix, bile duct, or pancreatic duct; and very rarely a worm may penetrate the wall of the intestine. The possibility must be recollected of damage by a roundworm to a suture line after bowel anastomosis.

It is wise to give anthelminthic treatment before operation whenever possible. The safest drugs at present available are compounds of piperazine. Piperazine adipate tablets each of 300 mgm. ("Entacyl," B.D.H.) may be used in an adult dosage of two tablets three times daily for seven days. Piperazine hydrate elixir containing 500 mgm. in each fluid drachm ("Antepar," B.W. & Co.) is used in a single dose of six drachms for an adult.

Hookworm Infection

(*Ancylostoma duodenale* and *Necator americanus*)

These small worms are found attached to the mucosa of the duodenum and jejunum from which they absorb blood. Heavy infections cause severe anæmia which will respond rapidly to oral administration of iron compounds when the worm load has been reduced. It is rarely possible to eradicate the infection completely but a few worms remaining are of no significance if re-infection is avoided.

After twelve hours' preliminary starvation the adult patient swallows hexyl-resorcinol 1 gm. in divided doses dispensed in rice-paper cachets. One hour later magnesium sulphate ½ ounce is taken, and when the bowels have acted the patient may take food again. Treatment for anæmia may be accomplished with ferrous sulphate compound ("Fersolate") one or two tablets with meals thrice daily for two or three weeks.

Tapeworm Infection

(*Tænia saginata* and *Tænia solium*)

The patient may notice the flat tape-like segments of the worm in his stools, or may find a segment which has migrated from his anus. The species of worm may be identified by examining with a lens a segment which has been compressed between two glass slides. The branched uterus is visible filling up the greater part of the segment. Usually there are many more than twelve lateral branches of the uterus when the segment is that of the beef tapeworm (*Tænia saginata*). Less commonly there are fewer than twelve lateral branches when the segment is that of the pork tapeworm (*Tænia solium*).

Treatment of these infections is most successfully accomplished when the patient is under supervision in hospital. It is necessary to empty the alimentary canal as completely as possible. The patient is starved for three days; solid foods are prohibited; weak tea, fruit juice and glucose drinks, and water are allowed. On each day magnesium sulphate ½ ounce is given to the adult patient. On the fourth morning liquid extract of male fern 100–120 minims made up to one ounce as a simple emulsion in glycerine is given in three divided doses to the patient. One hour later a further dose of magnesium sulphate ½ ounce is given. All bowel motions are washed through a metal gauze sieve and search is made for the head of the worm; a pin-head sized object at the end of a series of tiny segments. An alternative to treatment with male fern is by the use of mepacrine hydrochloride of which a suspension of 1 gm. in water is given in divided doses to the adult. The worm is then stained yellow, is contracted, and is often discharged intact.

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Cysticercosis

(*Cysticercus cellulosæ*)

When a patient is infected with the pork tapeworm (*Tænia solium*) it is possible for auto-infection to occur if the patient swallows eggs of the worm from his contaminated fingers. Alternatively it is believed possible that ova or a mature segment containing ova may be regurgitated from the intestine into the stomach. The action of gastric juice on the ova causes the release of the infective forms (hexacanth embryos) which re-entering the intestine and passing through its wall are carried by the blood or lymph channels to the liver, muscles, or other internal organs of the body. Thus the intermediate stage of development of the worm, normally occurring in the pig, occurs in man. This stage shows itself as small oval cysts (cysticerci) of 1–2 cm. in length. There may be some inflammatory reaction with fibrosis around them, and when they die calcium salts may be deposited in them. They are most often detected in the subcutaneous tissues where they can be palpated and from which one can be removed for examination, but they are also found in voluntary muscles, and internal organs such as the liver, heart, eye, and central nervous system. The calcified cystic opacities may be noticed at the time of a radiological examination. In most sites no symptoms are associated with their presence.

In the brain, however, a calcified cysticercus may cause attacks of Jacksonian epilepsy, or one may block the flow of cerebrospinal fluid at a Foramen of Munro, or in the third or fourth ventricle, so producing internal hydrocephalus. Since no medical treatments are effective, surgical measures may be discussed in relation to this cerebral form of the disease. Usually the fact that the cysticerci are numerous and diffusely distributed makes it impossible to undertake surgical removal of them.

Amœbiasis

Infection may result from swallowing live cysts of *Entamœba histolytica* in contaminated water or food. Flies can carry the cysts on to food. Uncooked food, especially that which requires much handling in its preparation, such as fresh salads, may be dangerous if the cook is a cyst-passer.

There are still some gaps in our knowledge of the natural history of amœbic infections, but the possibilities are that the infected person becomes a symptom-free cyst-passer for a short or a longer time, or that initially or subsequently he develops dysentery. Again, having been a cyst-passer, though not necessarily having had dysentery he may develop infection of the liver in the form of amœbic hepatitis or abscess. Contiguous extension may then occur to the pleura and lung through the diaphragm. Blood spread infection of other sites including the brain is uncommon. Following amœbic dysentery a localized granuloma may form in the wall of some part of the large intestine, commonly the cæcum or the descending colon. It is known as an amœboma. Rarely, the peri-anal skin in debilitated subjects of amœbic dysentery, or the skin adjacent to a discharging sinus from an amœbic abscess, may become infected by *E. histolytica*, resulting in extensive ulceration.

Amœbic Cyst-passer

For diagnosis, repeated stool examinations directly or by concentration methods (Ridley and Hawgood, 1956) should be made by one experienced in identifying *E. histolytica* cysts. The significance of the finding of such cysts in a person free from

symptoms is disputed, and it is probable that there are strains of *E. histolytica* of differing degrees of pathogenicity. In practice, especially where surgery of the alimentary tract is planned, it is wise to treat the infection.

During the treatment the patient should be confined to bed apart from using bathroom and lavatory facilities. A full diet is given concluding each day with a large meal (high tea) at 6 p.m. At 9 p.m. a sedative is given orally or parenterally; for most adults a hypodermic injection of soluble phenobarbitone 1 grain proves adequate. At 10 p.m. emetine bismuth iodide (E.B.I.) 3 grains in gelatin capsules is given. This routine is followed during a course of 10 days, and it will cure about 95 per cent of patients. A second course of treatment may be given after an interval of a month.

There are two common side-effects of the treatment: nausea and vomiting due to gastric irritation; and diarrhœa due to irritation of the large intestine. At the beginning of the course the patient may wake at about 2 a.m. feeling nauseated. He may retch or vomit a little fluid. In most cases only a few granules of E.B.I. will be vomited. If much of the drug is rejected an extra dose should be added at the conclusion of the course. The nausea usually diminishes after the first few nights. During the latter part of the course diarrhœa may be troublesome. Often it can be relieved by a simple kaolin and morphia mixture given orally, but it will subside entirely only after the completion of the course of treatment.

AMŒBIC DYSENTERY. The patient usually complains of several loose motions of the bowels daily, containing blood and mucus, associated with colicky abdominal pains, lassitude and loss of weight. Where ulceration affects the rectum, urgency of defæcation and rectal tenesmus may be severe. Under-nourished indigenous people in the tropics sometimes suffer from a fulminating type of amœbic dysentery characterized by severe diarrhœa, marked loss of weight, evidence of dehydration and electrolyte imbalance and a rapid downhill course. In many such cases there is a superadded bacillary dysentery. Some residents in the tropics suffer from chronic amœbic dysentery manifesting itself by lassitude and instability of the bowel function so that at one time there may be constipation, and at another some diarrhœa with blood and mucus in the stools provoked by dietetic or alcoholic excess. Patients in or from the tropics requiring surgical treatment for hæmorrhoids, fissure, or fistula-in-ano should always have careful investigations to exclude an underlying amœbic infection of the bowel, before surgery is undertaken.

Diagnosis depends upon a consideration of the history together with the result of a search for the causative parasite. Mucus from a freshly passed stool or taken from the bowel during sigmoidoscopy, should be examined at once for actively motile amœbæ containing ingested erythrocytes. At sigmoidoscopy in an early case pin-point yellowish necrotic spots on small erythematous elevations of the mucosa, the intervening areas of which are normal, represent the submucous necrotic foci caused by the amœbæ. In more advanced cases, however, ulcers may be seen, and in some of the most advanced, sloughs are present.

In cases of chronic dysentery during a quiescent phase when formed stools are being passed, speeding the passage of the intestinal contents by the use of a saline aperient will sometimes result in a fluid stool in which motile amœbæ can be found.

The control of the acute symptoms of amœbic dysentery is best achieved by the use of emetine hydrochloride given in a dose of 1 grain daily to an adult, by deep subcutaneous injection for 4–7 days. This should be followed by the ten-day course of E.B.I. which has

been described in treatment of the cyst-passer. Appropriate measures to correct dehydration and electrolyte imbalance may be required. The toxic effects of emetine and its compounds on the heart muscle, shown clinically by tachycardia, arterial hypotension, and sometimes collapse, have been over-estimated in the past. There is little danger of irreversible cardiac damage in the use of the doses recommended, provided that the patient is kept at rest. Danger arises when prolonged courses of these drugs are given or when they are given to ambulant patients.

AMŒBOMA. A patient who has had dysentery months or years previously may present himself with symptoms suggesting a recurrence of dysentery. On abdominal examination a tumour may be palpated, often in the area of the cæcum or sigmoid colon, but it may be anywhere in the large intestine. It is oval, firm, fixed, and slightly tender. Usually motile forms of *E. histolytica* can be found in the stools. Barium enema X-ray examination will show a filling defect at the site of the lesion, though it is not usually possible to differentiate this from the appearance due to a malignant growth. Occasionally excision of such a mass is performed and only after a report on the histology is it realized that the tumour was an amœboma.

In any case where there is a suspicion that the tumour could be an amœboma treatment should be given with emetine hydrochloride grains 1 daily for 7–10 days. An amœboma will resolve rapidly with this therapy. Later, a 10-day course of E.B.I. 3 grains daily should complete the treatment.

In the rare cases where a carcinoma is present in the large intestine of a patient suffering from intestinal amœbiasis, it will be found that dysenteric symptoms will improve under this treatment but the tumour will not diminish in size. Then laparotomy may be indicated.

AMŒBIC HEPATITIS. The patient, who may or may not give a history of amœbic dysentery in the past, complains of symptoms of fever often with rigors associated with lassitude, loss of appetite, loss of weight, and discomfort or pain in the right hypochondrium or the right lower chest. The temperature record will show intermittent or remittent pyrexia. On physical examination the enlarged tender liver can be felt and there are sometimes right basal crepitations. In many cases no parasites can be detected in the stools, though in some cases *E. histolytica* cysts are found. There is a leucocytosis: 20,000 to 25,000 white cells per cubic millimetre of blood, and an increase in the proportion of neutrophils. On X-ray screening usually the right hemidiaphragm is elevated and movement is reduced: a condition described as splinting of the diaphragm. Routine tests of liver function are normal. The value of an amœbic complement fixation test in this condition is still being assessed, but there is some evidence of more frequent positive results than in cases of intestinal amœbiasis.

In such a case the adult patient should be given a daily injection of emetine hydrochloride, 1 grain, for 4 days. In amœbic hepatitis all the acute symptoms rapidly improve with treatment. As soon as this occurs emetine may be stopped and treatment continued with tablets of one of the salts of chloroquine: chloroquine diphosphate or sulphate, each tablet containing 0·15 gramme base. An adult should have two tablets three times daily for two days followed by one tablet three times daily for at least 14 days. This substance, being concentrated in the liver destroys the parasites there. The only side-effect of significance is that patients have some difficulty with the power of accommodation while taking the larger doses. Following this course of treatment, the 10-day treatment with

E.B.I. should always be given to eradicate any residual intestinal infection, even though stool examinations have proved negative.

AMŒBIC ABSCESS OF THE LIVER. The initial symptoms and signs are those of amœbic hepatitis but when an abscess forms the intermittent or remittent pyrexia often settles and there are only occasional febrile attacks. Similarly the leucocytosis decreases and it is usual to find a total white cell count within or only slightly above the normal range. Enlargement of the liver occurs at the site of the abscess, so that a prominent, and sometimes fluctuant swelling may be palpable in the right hypochondrium; or the abscess may begin to point through the anterior abdominal wall, or in an intercostal space. There is the possibility of rupture of the abscess into neighbouring cavities: peritoneal, pleural, or pericardial. This danger is greater in the less common case of an abscess of the left lobe of the liver. Pain felt in the shoulder tip is due to involvement of the diaphragm. On radiological screening the hemidiaphragm on the affected side is elevated, motionless, and often shows "tenting" or irregularity of its contour. There is compression collapse of the adjacent area of lung.

It is possible for a small abscess to be absorbed, or, sometimes it becomes calcified and is detected years later at a radiological examination. On the other hand, it is common for secondary bacterial infection, usually with *Esch. coli*, to occur. The signs of pyogenic infection then become marked, with rigors, swinging temperature, and leucocytosis.

In any case where hepatic abscess is suspected it is wise to give preliminary treatment with emetine hydrochloride 1 grain daily by subcutaneous injection for 4–7 days. There will be rapid improvement in the general symptoms and signs in the case of an amœbic abscess. In addition there is a decrease in congestion of the liver which renders exploratory puncture of the organ less likely to cause severe hæmorrhage.

Exploratory Puncture of the Liver. The results of repeated aspiration of a liver abscess are better than those of open operation, but in the case of an abscess in the left lobe of the liver open operation is safer than exploratory puncture.

The usual site of puncture is in the right anterior axillary line in the eighth or ninth intercostal space unless there is a tender point or obvious pointing abscess into which the needle can be introduced. The skin is cleansed and the intended site is anæsthetised by local infiltration anæsthetic. The puncture can be performed with a wide bore needle attached to a syringe, or forming part of Potain's aspirator. The needle should be directed into various sectors of the right lobe of the liver in turn while gentle negative pressure is applied from the syringe or aspirator. If pus is obtained aspiration should continue until the cavity is empty. Aspiration may be repeated if signs point to a further collection of pus after a few days. The material is often of a reddish-brown colour, and is usually sterile on culture for bacteria. Amœbæ are not usually found for they are in the wall of the abscess, and appear in its contents only after the first aspiration has allowed more exudate to collect. Occasionally, the material is very thick and will not flow readily through the needle. Saline may be used to wash through the needle and to render more fluid the remaining contents of the abscess. If parenteral administration of emetine hydrochloride has already been started prior to aspiration, it is pointless to inject emetine into the abscess cavity.

Following aspiration, chloroquine should be given orally as described in the treatment of amœbic hepatitis, and this in turn should be followed by the 10-day course of E.B.I. which has been described for bowel infections.

been described in treatment of the cyst-passer. Appropriate measures to correct dehydration and electrolyte imbalance may be required. The toxic effects of emetine and its compounds on the heart muscle, shown clinically by tachycardia, arterial hypotension, and sometimes collapse, have been over-estimated in the past. There is little danger of irreversible cardiac damage in the use of the doses recommended, provided that the patient is kept at rest. Danger arises when prolonged courses of these drugs are given or when they are given to ambulant patients.

AMŒBOMA. A patient who has had dysentery months or years previously may present himself with symptoms suggesting a recurrence of dysentery. On abdominal examination a tumour may be palpated, often in the area of the cæcum or sigmoid colon, but it may be anywhere in the large intestine. It is oval, firm, fixed, and slightly tender. Usually motile forms of *E. histolytica* can be found in the stools. Barium enema X-ray examination will show a filling defect at the site of the lesion, though it is not usually possible to differentiate this from the appearance due to a malignant growth. Occasionally excision of such a mass is performed and only after a report on the histology is it realized that the tumour was an amœboma.

In any case where there is a suspicion that the tumour could be an amœboma treatment should be given with emetine hydrochloride grains 1 daily for 7–10 days. An amœboma will resolve rapidly with this therapy. Later, a 10-day course of E.B.I. 3 grains daily should complete the treatment.

In the rare cases where a carcinoma is present in the large intestine of a patient suffering from intestinal amœbiasis, it will be found that dysenteric symptoms will improve under this treatment but the tumour will not diminish in size. Then laparotomy may be indicated.

AMŒBIC HEPATITIS. The patient, who may or may not give a history of amœbic dysentery in the past, complains of symptoms of fever often with rigors associated with lassitude, loss of appetite, loss of weight, and discomfort or pain in the right hypochondrium or the right lower chest. The temperature record will show intermittent or remittent pyrexia. On physical examination the enlarged tender liver can be felt and there are sometimes right basal crepitations. In many cases no parasites can be detected in the stools, though in some cases *E. histolytica* cysts are found. There is a leucocytosis: 20,000 to 25,000 white cells per cubic millimetre of blood, and an increase in the proportion of neutrophils. On X-ray screening usually the right hemidiaphragm is elevated and movement is reduced: a condition described as splinting of the diaphragm. Routine tests of liver function are normal. The value of an amœbic complement fixation test in this condition is still being assessed, but there is some evidence of more frequent positive results than in cases of intestinal amœbiasis.

In such a case the adult patient should be given a daily injection of emetine hydrochloride, 1 grain, for 4 days. In amœbic hepatitis all the acute symptoms rapidly improve with treatment. As soon as this occurs emetine may be stopped and treatment continued with tablets of one of the salts of chloroquine: chloroquine diphosphate or sulphate, each tablet containing 0·15 gramme base. An adult should have two tablets three times daily for two days followed by one tablet three times daily for at least 14 days. This substance, being concentrated in the liver destroys the parasites there. The only side-effect of significance is that patients have some difficulty with the power of accommodation while taking the larger doses. Following this course of treatment, the 10-day treatment with

physiological or pathological state in the individual patient where greater intake of vitamins is necessary. Correction of deficiencies is best attained by attention to the diet as a whole. In surgical cases, however, vitamin supplements may be indicated. Vitamin C is necessary for the integrity of the intercellular cement substance of tissues. It is also utilized in the adrenal cortex. In this connection there is some evidence that, together with other glanular tissues such as the pancreas, the adrenals may be affected by protein malnutrition and that adrenal corticoids are reduced in amount. Possibly this factor, together with the great frequency of sepsis in wounds, is related to keloid formation, so common in many peoples especially in Africa. Since there is evidence of increased utilization of vitamin C in infections, and in wound healing, it is wise to supplement the surgical patient's diet by the administration of ascorbic acid 100 mgm. daily.

Post-operative Management and Febrile Complications. It is important to have obtained the patient's confidence before operation for repeated reassurance afterwards will be required. Many ignorant patients push their fingers under the wound dressing in an effort to find out what has been done to them, and sepsis may result. Again, whatever the surgeon's opinions about early ambulation in any particular case, he will often find his patient, unless completely immobilized by splints or bandaging, already ambulant several days before it was intended.

Pyrexia following closely upon a surgical operation in the tropics, as in a temperate climate should make one think of respiratory infections with lobar or lobular collapse, urinary infection, and wound infection. The investigation and treatment of these conditions are according to accepted general principles. In many parts of the tropics, however, the possibility of a malarial attack, and the possibility of some disturbance of the heat regulating mechanisms also should be considered.

Malaria

The patient has a rise in temperature during the course of a few hours, feels cold, and often shivers violently. There is then a brief time, about half an hour, when he feels very hot but the skin is dry. Headache, usually frontal and occipital in distribution is severe, and aching in the back and limbs is common. Next follows a period of marked perspiration and during the course of a few hours the temperature falls and the patient feels better apart from a feeling of exhaustion. Such pyrexial bouts occur on alternate days in the tertian types of fevers, and with two days free from fever in the quartan variety. But it must be recollected that in falciparum malaria (malignant tertian or subtertian) irregular pyrexia is common in the early stages and it may be several days before the typical pyrexial pattern is discerned. Further, in patients constantly exposed to re-infection more than one cycle of malarial development may be occurring in the patient's blood at the same time so that daily pyrexial attacks can occur. Since with each febrile attack many erythrocytes are destroyed anæmia will eventually become apparent. Splenomegaly is common but in indigenous people in an endemic area the spleen is usually firm and shows little alteration in size with subsidence of fever. The enlarged spleen is more exposed to trauma, and rupture spontaneously or following relatively minor trauma has been recorded on numerous occasions. Covell (1955) has reviewed this subject.

Confirmation of diagnosis in a case of pyrexia depends upon finding the malarial parasites in a drop of peripheral blood. The blood should be collected during the period

If open operation is performed it is important to provide a "cover" with emetine and chloroquine therapy beforehand, and during the time that a sinus is present, otherwise there is the danger of amœbic ulceration of the skin and subcutaneous tissue around the opening of the sinus.

(*b*) URINE EXAMINATION. Naked eye examination, routine chemical test of the urine, and microscopic examination of the deposit, preferably after centrifugation should be made.

In certain countries schistosomiasis is endemic, and the typical terminal-spined ova of *S. hæmatobium* may be seen with the low-power microscope. Notes on this condition are given later.

Urinary infections are very common and easily overlooked. Frequently the organism is of the *Esch. coli* group, and unless *in vitro* sensitivity tests indicate some other agent sulphonamide preparations should be used in treatment; for example, Sulphatriad 1 gramme thrice daily for 7–10 days with an increased intake of bland fluids.

(*c*) BLOOD EXAMINATION. As a routine it is wise to arrange for a hæmoglobin estimation, the examination of stained thick and thin blood films, and a leucocyte total and differential count. Many other investigations may be necessary in certain cases.

ANÆMIA

In tropical areas the commonest causes of anæmia are hookworm infection, to which reference has been made, and recurrent malaria.

PREVENTION OF MALARIAL ATTACKS. Many native patients show a few malarial parasites in stained thick films of blood. They are not suffering from a malarial attack, and in fact have some immunity or premunity to malaria. But stress, such as a surgical operation, may precipitate an acute malarial attack. Therefore during the time the patient is in hospital it is wise to give prophylactic treatment. For partially immune patients proguanil hydrochloride (Paludrine) 300 mgm. once a week is adequate. For non-immune patients 100 mgm. daily regularly while in the malaria area, and for 3 weeks after leaving it is the best preventive.

When parasitisation has been controlled the use of a simple iron-containing compound, given orally, for 2 weeks, will raise the hæmoglobin level.

PROTEIN DEFICIENCY

Large numbers of people in tropical areas exist on diets inadequate in quantity and quality of protein. These are poor subjects for surgery. While the correction of protein deficiency is a long-term matter, it is important that the surgeon should arrange for his patient to have a full diet, containing 100 grammes of protein daily, for as long as possible before operation, and during the post-operative period. Protein supplements such as skimmed milk powder or Casilan may be used to bring the protein intake up to the required level. It is noteworthy that where the serum albumin level is low and some œdema has occurred, an early effect of increased absorption of protein is a rise in serum albumin level, a loss of water from the tissues and so a preliminary fall in the patient's weight.

VITAMIN DEFICIENCIES

The occurrence of vitamin deficiencies, usually multiple in type, depends upon geographic, climatic, social, and religious factors as well as upon the occurrence of some

Typically, a person having little or no immunity to the local strain of *P. falciparum* in an endemic area, and who has had a few attacks of fever, takes quinine in small doses, and sometimes irregularly, as a preventive. Following exposure to cold or wetness, or sometimes after the stress of an operation, the patient experiences a chill for which he may take an increased dose of quinine: for example, 30 grains a day instead of his usual 5 grains a day. His temperature rises sharply to 104°–105°F., and he often has a rigor. There is pain in the renal areas of the back, and often severe vomiting. The urine may be normal in volume at first, but is dark reddish-brown in colour and contains hæmoglobin, protein, occasional erythrocytes and some hyaline and granular casts. Jaundice appears within a few hours of the onset. The spleen is enlarged and may be tender. The patient suffers from increasing pallor as the hæmolysis proceeds.

Repeated blood examination will show a rapid fall in the hæmoglobin level and in the erythrocyte count: as many as two million erythrocytes per cubic millilitre of blood may be destroyed in 24 hours. Parasites are often scanty or absent from blood films. The blood urea, and the serum bilirubin levels are raised. The common cause of death in the fatal cases is renal failure, and post-mortem examination of the kidneys shows cortical ischæmia and amorphous material in the tubules which may show degeneration of their epithelial lining.

Treatment of this condition must be without delay. The patient is kept absolutely at rest. If anæmia is severe blood transfusion should be started, or, if available, a transfusion of packed red cells in normal saline solution, but very careful cross-matching of donor's cells and recipient's serum, and the reverse test, are essential to avoid further hæmolysis. Dehydration makes the condition more serious, and is a consequence of severe sweating and persistent vomiting. A daily urinary output of 1200–1500 ml. is desirable and to attain this 2–5 litres of fluid must be absorbed daily. Fluids given orally or by intravenous drip infusion are required. The bladder must be emptied every four hours and a careful fluid balance chart maintained during treatment. If parasites have been found in the blood films it is wise to give chloroquine hydrochloride 0·4 gm. in 500 ml. of normal saline, by the intravenous drip. Later efficient malarial prophylaxis must be instituted and maintained. Trowell and Vaizey (1956) reported favourably on the use of Prednisone in blackwater fever.

Heat Exhaustion

Following surgical operation in the tropics, the patient may suffer from heat exhaustion, characterized by muscular weakness with cramps in the calves and feet, vomiting, reduced urinary excretion and a low urinary chloride concentration. During a long operation while draped in towels the patient may have sweated profusely. Pyrexia due to infections predisposes to the ill effects of heat. Usually the patient has increasing headache and anorexia with nausea and vomiting. Transient cramps may be experienced. Sweating continues. Sometimes the onset is more dramatic with vomiting followed by muscular cramps.

On examination the patient is exhausted, restless, and anxious. There may be little elevation of oral temperature but the rectal temperature may be up to 102°F. The pulse is usually rapid and of poor volume. The skin is pale, moist and cold. In more severe cases the physical signs are those of collapse. The urinary output is reduced and contains protein with hyaline and granular casts. The chloride content of the urine is reduced, or

of pyrexia, preferably when the temperature is rising. The patient's ear lobe or the tip of his finger is cleansed with ether or spirit and is allowed to dry completely. Glass slides must be dry and free from grease, having been washed with soap, and cleaned with a fat solvent before use. The site is punctured and a large pin-head sized drop of blood is collected near one end of a slide. The sharp straight edge of another slide is laid across the first slide, allowing the drop of blood to run across the width of the slide. The second slide, or spreader is now pulled or pushed steadily along the first slide making a thin film which dries in a second or two. A large drop of blood is then collected, in the middle of another slide and is smeared out with a needle to form a thick film about 1 cm. in diameter. Prior to staining, films must be kept covered to avoid dust and the activities of insects. It is usual to stain the thin film by Leishman's method, and the thick film by Field's method. These are then searched for parasites using the high power, and oil immersion lenses in the microscope. In a suspected case of malaria repeated blood films should be searched if parasites are not found on the first occasion.

The aim of treatment of malaria in the surgical patient in the tropics is to overcome the blood infection. For this purpose a rapidly-acting, safe, schizonticidal drug is needed, that is one which acts on the schizonts or dividing forms of the parasites in the blood. One of the salts of chloroquine: the diphosphate or the sulphate may be used. The tablets contain 0·15 gm. of chloroquine base. For a non-immune patient treatment of an acute malarial attack consists of 0·6 gm. base (4 tablets) on diagnosis, followed by 0·3 gm. six hours later, and then 0·3 gm. daily for 2 days. For partially immune patients a single dose of 0·6 gm. base will suffice. In many patients no further pyrexial bout due to malaria follows the exhibition of chloroquine, but sometimes one further, though usually mild, pyrexial attack occurs. Sometimes a patient seriously ill with falciparum (malignant tertian) malaria vomits repeatedly or becomes unconscious, and oral administration of drugs is temporarily impossible. Chloroquine hydrochloride 0·4 gm. base may be added to 500 ml. of normal saline and given during one hour by intravenous drip infusion. This method is required because rapid intravenous injection results in collapse with a marked fall in blood pressure. When the patient is sufficiently recovered to swallow drugs, oral administration may be used to complete the treatment.

An alternative to chloroquine is mepacrine hydrochloride 0·1 gm. tablets for oral use, and ampoules of powder 0·1 gm. and 0·3 gm. for intramuscular use. The course of treatment required in acute malaria in the non-immune adult consists of 0·3 gm. three times during the first day, 0·3 gm. twice on the second day, and then 0·1 gm. three times daily for 5 days. In the partially immune adult a single dose of 0 3 gm. to 0·5 gm. will be sufficient.

Where reinfection by malarious mosquitoes is possible, or in the relapsing forms of malaria due to *P. vivax*, *P. malariae* and *P. ovale*, a prophylactic or suppressive drug must be continued after the treatment for the acute attack. For this purpose proguanil hydrochloride is most adequte, used in the doses described under prevention of malarial attacks. *If pyrexia recurs, the blood films are negative, and one is satisfied that the patient* has ingested the doses of the drug recommended above, then search must be made for some other cause of pyrexia than malaria.

Blackwater Fever. This serious intravascular hæmolytic crisis in cases of falciparum malaria has become much rarer with the use of more efficient prophylactic drugs, and the less frequent use of quinine both in prevention and treatment.

Many methods of treatment for both active spreading and indolent ulcers are advocated. In some areas patients with such ulcers are *so numerous that their admission* to hospital blocks beds needed for other urgent cases. Hence methods which reduce the time required for in-patient treatment are very desirable, but it must be recollected by the advocates of occlusive dressings with Elastoplast or plaster of Paris, that the out-patient



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FIG 125 Tropical Ulcer on dorsum of the foot

so treated does not usually limit his activities and rest at home, and that where adhesive dressings can be opened the patient is very likely to uncover his ulcer to see what is happening to it.

Admission to hospital and treatment of the patient in bed is desirable during the acute phase of the ulcer. Antibiotics will control the infection. Most commonly penicillin is given: 250,000 units of crystalline penicillin by intramuscular injection followed by 300,000 units of procaine penicillin with aluminium monostearate (P.A.M.) once or twice in each 24-hour period for 3–4 days. Aureomycin $1\frac{1}{2}$–2 gm. a day in divided doses given by mouth for a similar period has proved successful in controlling the acute infections. Locally dressings with eusol are applied to remove sloughing material. Some

it may be absent. Where collapse supervenes anuria may develop and is of serious significance.

The consideration of the recent environment and the physical state of the patient and the recognition of lowered urinary chloride content point to the diagnosis. It is most important that a blood examination for malarial parasites should be made, and if they are present anti-malarial therapy must be given. A simple estimation of urinary chlorides can be used as a guide to treatment. A pipette with an attached rubber teat is used for measuring fluid amounts in drops, and must be washed carefully in distilled water after its use for each reagent. Into a test-tube are placed 10 drops of urine and 1 drop of 20 per cent potassium chromate solution. A 2·9 per cent solution of silver nitrate is now added drop by drop, counting the drops, until the solution turns brown. One drop is equivalent to 0·1 per cent (1 gm. per litre) sodium chloride in the urine. If less than 3 drops are required the patient is suffering from salt deficiency. If over 5 drops are needed there is no salt deficiency.

The patient must be kept in bed, and a detailed chart of input and output of fluid maintained together with readings of the urinary chloride content as a guide to treatment. A total of 5–6 pints of fluid with at least 25 gm. of salt, including that in foodstuffs, is required in the first 24 hours. Oral administration is safest. When the patient is vomiting repeatedly, or is unable to swallow fluids, parenteral administration is necessary. In severe dehydration 1 pint of isotonic saline may be given by intravenous infusion during 15–30 minutes, followed by a second pint in 30 minutes. The rate should now be reduced to 1 pint every 4 hours, but not more than 6 pints should be given in 24 hours, beyond which time oral administration of fluid and salt will usually be possible. In most cases the patient responds rapidly and makes a complete recovery.

Surgical Aspects of Some Diseases in Tropical Areas

Ulcers

Tropical Ulcer. This common ulcer is seen in hot and humid areas of the tropics affecting the foot and lower leg of patients whose limbs are exposed to minor trauma, and in many of whom malnourishment is a predisposing cause. Many organisms can be isolated from the acute ulcer, but it is believed that Vincent's organisms: a spirochæte and a fusiform bacillus, are important causative agents. Cancrum oris and noma are varieties of this infection in special sites.

In a few hours after a scratch or other trauma the part is swollen, painful, discoloured and may show a bulla filled with sanguinous fluid. There is rapid necrosis of the subcutaneous tissues and skin which slough leaving a red floor covered by sanguino-purulent matter of foul smell. General toxic symptoms and signs are usual at this stage. In many untreated cases the acute process subsides, sometimes having encircled the limb, and the ulcer becomes chronic or indolent. Partial fibrosis with early epithelialization at the periphery of the ulcer occurs, but the granulation tissue in the floor remains unhealthy and subject to reinfection with acute ulceration recurring over months or even years. When the ulcer is sited over a superficial bone such as the tibia reactive periostitis with new bone formation eventually occurs, and a chronic ulcer then may lie over a mound of new bone so that the granulation tissue of the ulcer base is thin and poorly supplied with blood, and consequently healing cannot be completed.

Many methods of treatment for both active spreading and indolent ulcers are advocated. In some areas patients with such ulcers are so numerous that their admission to hospital blocks beds needed for other urgent cases. Hence methods which reduce the time required for in-patient treatment are very desirable, but it must be recollected by the advocates of occlusive dressings with Elastoplast or plaster of Paris, that the out-patient



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favour the use of bismuth subnitrate, iodoform, and paraffin paste (BIPP) or a modification in which zinc peroxide replaces the bismuth compound. The ulcer should be cleaned and its surface dried before the paste is applied, and a firm dressing and bandage should be left intact for 5–7 days. Others favour Elastoplast, adhesive plaster, or Viscopaste occlusive dressings at this stage. These may be left in place for one to two weeks if possible. In many cases healthy granulations form and epithelialization proceeds satisfactorily under such dressings.

Some acute ulcers on the lower leg, and many of the chronic ulcers, especially those over areas of bony thickening can be treated by radical excision and skin grafting. The limb should be prepared while the ulcer is kept covered. General or spinal anæsthetic is suitable. In the latter case a "light" solution in small dose is injected intrathecally and the patient maintained thereafter with the lumbar area elevated above the level of the neck and head. Retaining a firm covering over the ulcer surface, its skin edges are treated with a disinfectant such as tincture of iodine. An incision is made at about ½ in. from the ulcer edge, circumferentially, and entering the subcutaneous tissue. Four, or more, tissue forceps are attached with one blade in the incision and one in the gauze-covered ulcer. By lifting these and under-cutting its base the ulcer can be removed completely without any contaminated instruments having touched the newly exposed surface. The rapid bleeding which usually occurs can be controlled in most cases by firm pressure with a pack soaked in hot sterile saline. Only rarely is it necessary to take more active measures to secure hæmostasis. Where bony overgrowth is present it can be chiselled away leaving a flat or slightly concave surface across which granulations can grow. When bleeding has ceased a sterile Vaselined gauze dressing may be applied with a pad of wool and firm bandaging, and the wound may be left for a week. At the end of that time healthy granulations will usually be found to which Thiersch grafts or pinch grafts can be applied with reasonable assurance that they will grow. Thus in a favourable case a patient may be discharged with the ulcer healed in less than three weeks.

GUINEA WORM INFECTION (*Dracunculus medinensis*). In local areas, where incidence may be very high, guinea worm infection is found around the tropical and subtropical zones, particularly in West Africa, Persia, and India. Infection is acquired by drinking water, often drawn from wells, containing the intermediate host of the worm; a crustacean named *Cyclops*. The adult female worm, which may be a metre in length, migrates in the tissues and approaches the body surface commonly on the ankle or leg, but occasionally at other sites, when she matures.

At that time the patient may be troubled by allergic phenomena, urticarial eruptions, vomiting, and local pain. There is eosinophilia. At the site where the head of the worm will appear an indurated papule forms, on the surface of which a vesicle appears. When this ruptures a shallow ulcer is seen, in the floor of which is a sinus from which protrudes a whitish thread-like structure; the head and opened uterus of the worm. Cold applications result in reflex contraction of the worm the outline of which approaching the ulcer may then be seen or palpated more easily, and in the discharge into the ulcer of a milky fluid which contains thousands of the embryos of the worm. The adult worm is lying in a tunnel of the subcutaneous tissues, often with some fibrous tissue reaction around it, and attempts to pull out the worm will be unsuccessful until parturition is complete, which may require repeated cold applications to the ulcer surface for as long as three

weeks. The most important complications of guinea worm are due to secondary infection commonly by staphylococci. Cellulitis may occur, and abscesses may form along the tunnel occupied by the worm. These complications are much more likely if the worm is broken off and retracts into the tissues after unsuccessful attempts at removal. Sometimes the worm dies in the tissues and becomes calcified when it may be palpable as a hard linear cord, or it may be seen by chance on a radiograph. Treatment follows traditional practice supplemented by the use of the newer antibacterial agents. Sterile cold compresses should be applied until no further milky fluid is ejected by the worm. A silk thread is now used to attach the protruding worm to a glass rod or small stick. By very gradual intermittent traction the worm may be drawn out, and rolled on to the rod. Antibiotics must be used for secondary infection. Fairley (1925) used more active surgical measures to remove the worm. The worm is outlined by spraying ethyl chloride on to the skin surface which causes a vigorous contraction. Using local anæsthesia, after preparation of the skin surface, small transverse incisions are made across the line of the worm. By means of a squint hook the worm may be drawn up into each wound, divided, and removed in sections, taking care that the distal section is withdrawn through the original sinus in the floor of the ulcer. Thus, in a successful case, the time required to remove the worm is greatly reduced.

ORIENTAL SORE (Cutaneous Leishmaniasis). The numerous local names of this condition indicate its distribution in the Middle East from south-eastern Russia to the Indian continent, but it is also found in Central and South America. The causal organism, *Leishmania tropica*, is transmitted by sandflies of the genus *Phlebotomus*. The sores, usually single, sometimes multiple, occur on exposed parts, or are due to direct inoculation of material from a sore into abrasions. Because an immunity develops after infection, and because the sores heal with scarring which is obvious and may be deforming, for example on the face or eyelids, the practice has arisen in some parts of the East of deliberate inoculation of a child on an unexposed area of its body in the hope of limiting the disease to this site.

The infective form of the parasite is an elliptical flagellated leptomonad, and it is this form which appears in successful cultures of material from a sore. In the tissues the parasites become rounded in form and non-motile, and are found inside reticulo-endothelial cells. These are Leishman-Donovan bodies. Some months or even two or three years may elapse between the time of an infected bite and the appearance of a lesion at the site. A reddish itchy papule forms and increases in size and nodularity. Its centre ulcerates. Secondary infection is common and a dried crust forms in the ulcer cavity. Occasionally inoculation into nearby skin results in other similar lesions near the first, and these may coalesce, but usually the sore is not more than 1 in. in diameter. Eventually natural healing by fibrosis occurs. In south-eastern Russia and Turkestan the commoner type of lesion is a warty, papillomatous dry growth. Constitutional disturbances do not occur due to cutaneous leishmaniasis.

Diagnosis depends upon recollecting the area of residence of the patient, noting the appearance of the chronic ulcer on a raised slightly nodular base, and upon identifying leishmanial parasites in a smear of cells and tissue fluid from the base of the ulcer or after culture of such material. To obtain a specimen for examination puncture is made into the base of the ulcer through the skin margin so as to avoid contaminated matter in the ulcer

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At that time the patient may be troubled by allergic phenomena, urticarial eruptions, vomiting, and local pain. There is eosinophilia. At the site where the head of the worm will appear an indurated papule forms, on the surface of which a vesicle appears. When this ruptures a shallow ulcer is seen, in the floor of which is a sinus from which protrudes a whitish thread-like structure; the head and opened uterus of the worm. Cold applications result in reflex contraction of the worm the outline of which approaching the ulcer may then be seen or palpated more easily, and in the discharge into the ulcer of a milky fluid which contains thousands of the embryos of the worm. The adult worm is lying in a tunnel of the subcutaneous tissues, often with some fibrous tissue reaction around it, and attempts to pull out the worm will be unsuccessful until parturition is complete, which may require repeated cold applications to the ulcer surface for as long as three

therapy, or the application of diathermy have been tried with varying success. In suitable sites complete excision of the lesion may be performed. Where there are numerous sores parenteral treatment as for visceral leishmaniasis with antimony or diamidine compounds may be tried.

DESERT SORE. The term desert or Veldt sore is used for various chronic ulcers occurring on exposed parts, especially the feet and legs, forearms, and backs of the hands of those who must travel in hot desert areas without means to keep their skin surfaces regularly cleaned. They occur in parts of north and south Africa, north Australia and other climatically similar areas.

The lesion commonly commences as a vesicle on a painful erythematous base. When the vesicle ruptures the ulcer increases in size and depth and it often has a greyish membrane on its surface. The edges are unhealthy and overhanging, and a dry scab may form in the ulcer crater. These sores are often resistant to simple local therapy applied while the patient's mode of life is unchanged. While hæmolytic streptococci can be isolated from most of these ulcers, in some diphtheria bacilli have been found, and diphtheritic paralyses are recorded in association with some of them. Treatment may be successful if local measures, such as the use of acriflavine dressings, or the application of Elastoplast for a few days, are conscientiously applied. Where diphtheria organisms are found or suspected an intramuscular injection of 20,000 units of antitoxin should be given. Parenteral administration of penicillin, if necessary with bed rest for the patient, will usually cause healing, but occasionally resort to surgical excision of the ulcer followed by skin grafting is necessary.

ULCERATIONS IN SICKLE-CELL ANÆMIA. It is noteworthy that patients having sickle-cell anæmia, an inherited abnormality of the erythrocytes which in conditions of reduced oxygen tension become elongated and crescentic or sickle-shaped, suffer from multiple thromboses in various organs and tissues of the body. This may manifest itself as chronic recurring ulceration of the legs. As yet, apart from carefully matched transfusion as an emergency procedure, there is no specific treatment for this disorder, and the ulcers must be treated according to general principles.

MYCETOMA. Mycetoma or maduramycosis is a chronic granulomatous condition commonly of the foot, but occasionally of other sites, associated with swelling, deformity and destruction of the tissues, and eventually the presence of several sinuses from which a mucoid discharge escapes, containing "grains" which are red, yellow, or black and are formed of masses of the causative fungi. There are many ærobic fungi of the genus Nocardia which have been identified as causal agents. The condition is found in India and in Africa but cases have been described from most areas of the tropics and subtropics. The patient, usually a peasant farmer who is bare-footed, complains of painless swelling of the foot. It may be well or ill-defined. There may be the history of a punctured wound with a thorn, but such injuries in people of this group are so common as to pass unremembered. Once established mycetoma grows slowly but steadily. There is remarkably little pain and consequently most patients seek help late in the development of the disease when sinuses have formed which become secondarily infected. Abbott (1956) points out that black mycetoma due to *Madurella mycetomi* remains localized and encapsulated until late in its development, spreading along tissue planes and only

cavity. A finely drawn glass Pasteur pipette may be pushed into the wall of the ulcer from the skin surface and a little tissue fluid obtained by capillary attraction or by gentle suction with a rubber teat, or a dry syringe and needle may be used in the same way. The material obtained should be spread on a clean slide, dried, and stained by Leishman's or Giemsa's method. The typical appearance under the high power microscope is of



FIG 126 Oriental Sores (Cutaneous Leishmaniasis) on nose and chin (*Prof. A. W Woodruff*)

numerous minute ovoid bodies in the large mononuclear cells. Material so obtained, or taken from a biopsy of the ulcer edge, may be placed in N.N.N. medium and kept at room temperature. Repeated examination of a drop taken from the culture tube should be made until leptomonad forms are found, or three weeks have elapsed.

Various treatments have been used to stimulate the healing of oriental sores. The one used depends in part upon the site of the sore. In any case the usual measures to overcome secondary pyogenic infection are of great value. Injection at points beneath the floor of the ulcer of 1–2 ml. of various solutions may increase reaction: 2 per cent berberine sulphate, 5 per cent emetine hydrochloride or 5 per cent mepacrine have been used. Carbon dioxide snow applied for a very short time at intervals of 10 days; X-ray

regions is seen, particularly in women, in most tropical areas. Infection occurs during sexual contact. About a week later a painless papule or vesicle which ulcerates may be noticed on the genitalia, unassociated with lymphadenopathy. Ulceration slowly extends, affecting especially the moist areas, and remaining in the skin, subcutaneous tissue or mucous membranes. Healing by fibrosis in some areas with chronic ulceration in neighbouring areas, but without lymph gland involvement, is characteristic. Eventually the genitalia are deformed by fibrosis which, especially in the female, may result in stenosis of the urethra, vagina, or anus, and in a condition like elephantiasis due to fibrous tissue overgrowth and lymph stasis. Rectovaginal fistulæ may form when ulceration has extended to this region.

Diagnosis depends upon recognizing the lesions, and may be confirmed by finding Donovan bodies: small round ended bodies inside large mononuclear cells, in a stained smear of material obtained by scraping the ulcerated surface.

Treatment consists in local applications to overcome secondary infection, in the use of certain antibiotics, and sometimes in surgical measures to treat strictures, fistulæ, or pseudo-elephantiasis. Streptomycin by intramuscular injection in doses up to 4 gm. per 24 hours for 5 days; chlortetracycline by mouth in 250 mgm. capsules every six hours to a total of 15–20 gm.; or chloramphenicol given orally in doses of 3 gm. daily for 10–12 days, have each proved successful.

Swellings and Lymph Gland Enlargements

Filarial Swellings

A number of species of filarial worms may infect human beings in different parts of the world, and in most of these infections swellings of various kinds occur. Reference is made below to the most important of these filarial infections.

Loiasis. *Filaria Loa loa* is transmitted by the bite of an infected Mango fly (*Chrysops* species) found in the forest margin areas of West Africa, particularly in Eastern Nigeria and the Cameroons. Clinical manifestations of the infection consist in the appearance of Calabar swellings, and the appearance of an adult worm beneath the skin or migrating across the eye under the bulbar conjunctiva. Calabar swellings are diffuse, firm, usually non-painful, and transient swellings commonly about 5 cm. in diameter appearing on the dorsal surfaces of the hands and forearms especially after active use of the fingers, on the face, and sometimes on other sites. The swellings may remain for a few hours up to 2 or 3 days, rarely as long as a week.

Investigations of a patient with such findings will usually show that there is an eosinophilia, and during the hours near midday sheathed microfilariæ may be found in the peripheral blood. The more blood that can be examined the better is the chance of finding microfilariæ and various concentration techniques using several millilitres of blood have been devised. Supporting evidence of filariasis may be obtained by an intradermal sensitivity test, and by a complement fixation test. The disease may be a cause of economic loss to a patient, but is not usually associated with serious complications though Schofield (1955) reported nerve damage in the forearm in patients suffering from loiasis.

Treatment is successful using di-ethylcarbamazine ("Hetrazan" or "Banocide") supplied in 50 mgm. tablets for oral administration. The dose, calculated according to

invading muscles and bones later. In this earlier phase surgical dissection and excision is possible. Yellow mycetoma due to *Nocardia somaliensis* and Red mycetoma due to *N. pelletieri* were, in his experience, less well-defined in their earlier growth and infiltration of muscle occurred early so that excision of infected tissue was less likely to eradicate the disease.

Diagnosis depends upon recognizing the possibility of the disease, which causes painless firm nodules and eventual enlargement and deformity of the affected part. In



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FIG 127 Ulcerating Granuloma of the pudenda (Donovanosis)

the early stages fungus can only be obtained by taking a portion of tissue for section and culture. When sinuses have formed the granules in the discharge indicate the diagnosis which is confirmed by examination of one of these under the microscope or by culture on Sabouraud's agar medium. Growth is on the surface of the medium, and branching, septate hyphæ are found with large chlamydospores (Mackinnon, 1954). Radiological examination may show rarefaction of bones, sometimes with some new bone formation. Cystic spaces may be seen in the bone, and at operation these are found to be filled by granules of the fungus.

Treatment consists in attempts at surgical dissection and excision of the infected tissues in the early case. Secondary infection must be treated on accepted principles, and will often result in great improvement in the local condition but relapse is inevitable. Chemotherapy with oxytetracycline and carbomycin has been reported to produce temporary improvement (Abbott, 1956) and further trials are justified in view of the fact that in the final stage, amputation of the affected part is the only alternative.

ULCERATING GRANULOMA OF THE PUDENDA (Granuloma venereum). This condition of chronic, progressive granulomatous ulceration with fibrosis of the genital and inguinal

regions is seen, particularly in women, in most tropical areas. Infection occurs during sexual contact. About a week later a painless papule or vesicle which ulcerates may be noticed on the genitalia, unassociated with lymphadenopathy. Ulceration slowly extends, affecting especially the moist areas, and remaining in the skin, subcutaneous tissue or mucous membranes. Healing by fibrosis in some areas with chronic ulceration in neighbouring areas, but without lymph gland involvement, is characteristic. Eventually the genitalia are deformed by fibrosis which, especially in the female, may result in stenosis of the urethra, vagina, or anus, and in a condition like elephantiasis due to fibrous tissue overgrowth and lymph stasis. Rectovaginal fistulæ may form when ulceration has extended to this region.

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Treatment is successful using di-ethylcarbamazine ("Hetrazan" or "Banocide") supplied in 50 mgm. tablets for oral administration. The dose, calculated according to

the patient's weight in kilogrammes, is begun at 3 mgm. per kilogramme per day, and after 2 days is increased to 6 mgm. and after a further 2 days to 9 mgm. per kilogramme per day. At this level the dosage is continued to complete an over-all course lasting 21 days. Reactions and side-effects of treatment are minimal, though an adult worm may migrate up to the skin surface and die there, when it may be removed surgically, or when it will eventually be absorbed.

ONCHOCERCIASIS. Infection by *Onchocerca volvulus* found in West Africa, particularly in Ghana, in parts of East Africa, and in Central America, is due to bites by infected Buffalo gnats (*Simulium* species). The degree of infection depends upon the number of parasites which survive in the body of the human being, and consequently the heaviest infections occur in indigenous inhabitants of endemic areas. The three clinical manifestations of the disease are itching, macular or papular, erythematous rash progressing to lichenification commonly seen on the back of the shoulders, buttocks, and outer aspects of the thighs and arms; recurrent conjunctival injection with punctuate keratitis and diminished visual acuity, progressing to corneal opacity and blindness in severe cases; and onchocercal nodules. These are sessile or pedunculated, firm nodules of a few millimetres to several centimetres in diameter most often first noticed over bony prominences such as the iliac crests, the costal margins, and on the head. They are formed of fibrous tissue enclosing coiled adult male and female worms, and from nodules containing live worms it is believed microfilariæ migrate out into the skin, or conjunctiva, causing the other clinical manifestations of the disease.

Diagnosis is supported by the finding of an eosinophilia and by the group tests for filariasis: the skin sensitivity test, and the complement fixation test. It is confirmed by finding microfilariæ, or an adult worm in tissue removed from the patient. Skin shavings, made as though one were taking thin Thiersch grafts, from various areas especially near a nodule or where there is a rash, may be examined in normal saline under the low-power microscope. Motile unsheathed filarial embryos may be seen in the skin or the saline. A fragment of bulbar conjunctiva taken after local surface anæsthesia, may be examined in the same way. If a corneal microscope is available microfilariæ may be identified in the cornea or anterior chamber of the eye. A nodule may be punctured and tissue fluid examined for microfilariæ, or nodules may be excised for histological examination. At the time of operation the cut surface of the freshly excised nodule may be rubbed on to a clean slide which again may be examined at once for microfilariæ.

Treatment for this disease is with di-ethylcarbamazine ("Banocide") as described for loiasis. However reactions in the form of increased skin irritation and, if the eyes are involved, increased conjunctival injection and irritation are common at the beginning of treatment. Consequently it is usual to begin the treatment at a dosage level of 1 mgm. per kilogramme per day if it is suspected that the eyes are affected. When reaction from this dose has subsided the level may be increased gradually to the scale described under the treatment of loiasis. In onchocerciasis, however, bigger doses are often used, reaching 12 mgm. per kilogramme per day, but the course of treatment is again usually 21 days. Reactions may be controlled by the use of antihistamines given concurrently with Banocide (Anthisan 100 mgm. twice daily with Phenergan 25 mgm. each evening). In cases of reaction of the eyes Cortisone eye drops (5 per cent cortisone acetate) prove valuable.

Since the adult worms being enclosed by fibrous tissue may not be destroyed by this course of treatment, other methods of treatment have been advocated. Intravenous injections of Antrypol (Suramin) may be given concurrently with Banocide or as a separate course of treatment. The urine of the patient must be tested before each injection since toxic effects on the kidneys, as revealed by proteinuria with a deposit containing cellular casts and sometimes erythrocytes may occur. A trial dose of 0·2 gm. is given intravenously to detect idiosyncrasy to the drug. Then 1 gm. may be given once weekly to the adult patient for 5 weeks.

Finally, surgical excision of nodules, especially when these are numerous, and especially when they are on the scalp or face, is a valuable means of removing some adult worms.

BANCROFTIAN FILARIASIS. In many parts of the tropical and subtropical zones infection by *Wuchereria bancrofti* occurs, the insect vectors being mosquitoes of the genera *Culex*, *Aedes* and *Anopheles*. Adult filarial worms may be found in lymph glands particularly of the inguinal and para-aortic groups. Sheathed microfilariæ may be found in the peripheral blood in greatest concentration between the hours of 10 p.m. and 2 a.m., when the insect vectors are most active. Some related filarial parasites do not show this nocturnal periodicity the exact cause of which is still unknown.

Clinical evidences of infection are mostly due to the presence of adult worms in the lymphatics, though some symptoms and signs are probably due to an allergic reaction to the adults or embryos. Late results of Bancroftian filariasis are most often seen in indigenous people of endemic areas and it is believed that repeated infection is an important factor in causing these. The early clinical evidences of infection are attacks of filarial fever commonly associated with lymphangitis and lymphadenitis sometimes with abscess formation especially in the inguinal region, and funiculitis, orchitis and hydrocœle in the male. The lymphangitis is typically centrifugal or retrograde with red marks progressing distally down a limb.

Following several such febrile attacks the later clinical evidences appear, due to lymphatic obstruction by fibrous tissue formation in the glands and round the lymph vessels. The transient œdema occurring in the early attacks later becomes permanent. Then progressive enlargement of the limb occurs, with thickening and folding of the skin. Recurrent bacterial infection of the skin is common and adds to the fibrosis around and in lymph glands. While these changes commonly affect the legs, in some cases the arms are affected, and in women the breast or vulva may be involved. Chronic lymph stasis in the male may result in lymph scrotum, a condition in which vesicles form on the scrotal skin, and if these rupture a discharge of lymph occurs in a site where recurrent secondary infection is to be expected. Large hydrocœles with thick walls are common, and in some cases the whole scrotum becomes grossly thickened, and enlarged. Its weight stretches the pubic and inguinal tissues, and the penis is buried in the anterior wall of the swelling. Sometimes obstructed lymphatics carrying chyle in the lower abdomen may rupture into the pelvis of the kidney, ureter, or bladder resulting in chyluria; they may rupture into the peritoneal cavity resulting in chylous ascites.

Diagnosis in the earlier stages of the disease depends upon the history of the patient's residence in an endemic area of filariasis, and the history of attacks of filarial fever with

diagnosis is confirmed when embryos are recovered from the blood collected at about midnight. Occasionally Bancroftian filarial embryos are found in fluid obtained on tapping a hydrocœle and sometimes they are seen in the deposit from chylous urine. In the later stages of the disease, while the history may be suggestive of filariasis, and the signs of chronic lymphatic obstruction are found, evidences of active filarial infection such as eosinophilia, a positive complement fixation test, and the finding of live embryos, may not be obtained. The skin test may give supporting evidence however, since once it becomes positive it is likely to remain so for years, or even for life. Radiological examination may reveal calcified filarial worms in lymph glands; and sometimes histological examination of a gland removed for section shows the presence of a worm.



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Fig. 128 Late effects Bancroftian filariasis showing inguinal adenopathy, hydrocele, and elephantiasis of the leg

Treatment for active Bancroftian filariasis is by oral administration of di-ethylcarbamazine ("Hetrazan" or "Banocide") as has been described in cases of loiasis. It is usual, however, to increase the dose to a maximum of 12 mgm. per kilogramme body weight per day. This will destroy embryos in the blood, and may destroy adult worms, though a second similar course of treatment may be required.

Where elephantiasis has occurred a course of Banocide may be desirable to eradicate possible active infection but it will not improve the obstruction to lymph drainage. The common occurrence of secondary infection makes bed-rest, elevation of the affected limb, and parenteral administration of penicillin necessary means of therapy. Attempts to restrict the progressive enlargement of a leg consist in elevation to assist drainage, and then the provision of a measured elastic stocking which the patient should put on before getting out of bed each morning, and wear till returning to bed each evening.

For gross elephantiasis, where the weight and size of the part are a burden and severe deformity to the patient, operative interference may be required. Amputation of affected parts may be necessary, as in the case of the breast, the enlarged labia, and the

scrotum. In these cases the pre-operative preparation of the skin is very important. Where possible the part should be elevated before operation so as to reduce its bulk. The surgeon must recollect that the tissues are hypertrophied as well as œdematous, and consequently large blood vessels are likely to be encountered during the operation. In the case of the scrotum it is very important that the presence of a large inguinal hernia should have been considered as the possible explanation of the scrotal swelling. It is also important to realize that in patients with elephantiasis of the scrotum large thick-walled hydrocœles will be encountered as the operation proceeds. The elongated spermatic cords and the testes, after excision of the thickened tunica vaginalis are buried beneath the skin flaps which form the scrotal repair. Where secondary infection is prevented or controlled healing of the tissues proceeds satisfactorily.

Various operative procedures have been attempted for elephantiasis of the legs. They should be undertaken only when it is clear that the conservative measures described above have failed, and where the bulk of the limb is a serious hindrance to the patient. In these circumstances the operative procedure consists in excising as much as possible of the œdematous and fibroid subcutaneous tissue of the leg and allowing the skin flaps which have been made to return as whole-thickness grafts. The result is a less bulky limb, but one having irregular contours. Consequently a warning about this is necessary for any patient hoping for cosmetic improvement of an elephantoid limb. The difficulties of the operation are hæmorrhage, sepsis with devitalization of the skin flaps, and the difficulty of excising an adequate amount of thickened tissue from the foot. Various attempts by the construction of grafts from parts of the trunk down to the leg in an effort to provide new pathways of lymph drainage have not been very successful. There is scope for investigation of the pathology of the lymphatics in these cases, and interesting papers may be read on the injection and transport of dyes by the lymphatics, by Hudack and McMaster (1933) and by Kinmonth (1952) and Kinmonth and Taylor (1954).

Adenitis

Among the many possible causes of lymph gland enlargement the surgeon in tropical practice should consider the following.

Tuberculous Adenitis. Native patients often exhibit a different clinical picture of tuberculous infection from that usually seen in temperate areas. This is probably related to differences in resistance to the infection, and the different age at which infection is first acquired. Patients may be seen who suffer from persistent pyrexia of which the cause is obscure. Only after some weeks are enlarged lymph nodes found, and if one is removed for section the histological appearances of tuberculosis are found. Other patients develop enlarged glands which caseate and break down in a site not commonly first showing tuberculous adenitis, such as in the inguinal region.

Syphilitic Adenitis. The primary sore of syphilis, particularly in the male patient in the tropics, is often infected with pyogenic organisms. The resulting ulcer is larger and deeper than the typical primary chancre; and regional lymph nodes are enlarged, painful and tender, and may suppurate.

Adenopathy in Mite-borne Typhus. Infection by *Rickettsia orientalis* occurs in rodents in areas of Japan, China, Burma, Malaya, the East Indies, and New Guinea. These rodents harbour mites of the genus *Trombicula*. The larval mite takes one blood

diagnosis is confirmed when embryos are recovered from the blood collected at about midnight. Occasionally Bancroftian filarial embryos are found in fluid obtained on tapping a hydrocœle and sometimes they are seen in the deposit from chylous urine. In the later stages of the disease, while the history may be suggestive of filariasis, and the signs of chronic lymphatic obstruction are found, evidences of active filarial infection such as eosinophilia, a positive complement fixation test, and the finding of live embryos, may not be obtained. The skin test may give supporting evidence however, since once it becomes positive it is likely to remain so for years, or even for life. Radiological examination may reveal calcified filarial worms in lymph glands; and sometimes histological examination of a gland removed for section shows the presence of a worm.



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For diagnosis the history and clinical signs of the condition are a guide, and supporting evidence is obtained if the Frei test is positive. An antigen containing heat-killed



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FIG 129 Lymphogranuloma inguinale (Climatic Bubo).

virus is injected intradermally. The test should be read at 48 hours. If positive there is an infiltrated inflammatory swelling at least 5 mm. across, following the injection of 0·1 ml. of antigen. The nodule persists for 2–3 weeks. The Frei test is likely to remain positive for many years after infection, so that a positive reading must be interpreted in the light of the clinical data. In some laboratories a complement fixation test on the patient's serum can now be used as evidence of infection.

In the early case complete rest in bed may allow resolution of the affected glands. If fluctuation of the swelling is present aspiration under strict aseptic precautions may be performed. Chlortetracycline may be given orally in a dose of 2 gm. every 24 hours, for 10 days. Where fistulae or strictures have formed, or where elephantoid swelling following fibrosis causes complications, surgical measures may be necessary, but should be preceded by the course of medical treatment which has been outlined.

SCHISTOSOMIASIS

The majority of human infections by the trematodes known as blood flukes are caused by *Schistosoma hæmatobium*, *S. mansoni*, and *S. japonicum*. The disease may be acquired by contact with water containing infective forms (cercariæ) of these flukes.

meal during its development, but if this is infected, transovarian transmission occurs so that the larval mites hatching from the eggs of this mite are already infective. They tend to migrate upwards, and in humans the sites of bites are the thighs and buttocks, and the upper arms or neck. At the site of the bite a small papule forms which may develop into an ulcer 2–4 mm. in diameter, in which is a dried black slough, and around which is a dull erythematous zone. The regional lymph glands are enlarged but are not usually tender. The onset of the illness is generally sudden after an incubation period of 1–2 weeks following the bite. The eschar, or site of the bite, takes 3–4 weeks to heal, so that in a case of sudden febrile illness in the areas mentioned a physical examination may reveal regional adenopathy, and further search in the part drained by this group of glands may show the eschar. Later in the illness more generalized adenopathy may occur. Early treatment with chlortetracycline, oxytetracycline, or chloramphenicol will bring about a rapid cure in most cases.

Bubonic Plague. In many tropical areas plague is an enzootic of rodents, the causal organism *Pasteurella pestis* being transmitted by fleas which infest the rodents. Sporadic cases or epidemics of plague in humans result from an extension of the disease first to rats, particularly those which live in or near human dwellings. The rat flea *Xenopsylla cheopis* is the most important vector.

The onset of bubonic plague is sudden and severe with fever, disorientation, and prostration. On the second or third day an exquisitely tender bubo forms. Before swelling is apparent there may be marked tenderness at the site. Most commonly this is the femoral or inguinal group of glands, less commonly the axillary or cervical glands are affected. The glands may suppurate after about 2 weeks.

Diagnosis depends upon puncturing the bubo and obtaining material for smears and for culture. The organisms are short, Gram-negative rods showing bipolar staining. They are easily grown in culture.

General measures of treatment are important and consist in bed rest, fluid diet, and hot fomentations or kaolin poultices to the bubo. Favourable results have followed treatment with streptomycin together with sulphadiazine. A suitable regimen is: streptomycin by intramuscular injection 0·25 gm. to 1·0 gm. every 4 hours until the temperature is normal. Sulphadiazine is given orally at the same time: 4·0 gm. as a loading dose, followed by 2·0 gm 4 hours later, and then 1·0 gm. every 4 hours until the temperature has been normal for 2 days.

Lymphogranuloma Inguinale (Climatic Bubo). This venereal disease occurs in many parts of the world especially in the great seaports of the tropics and subtropics. It is caused by infection with a virus, and manifests itself as a small and often disregarded herpetiform ulcer on or near the genitalia occurring from a few days up to 3 weeks after infection. After 2–3 weeks swelling of the regional lymph glands occurs. In the male it is the inguinal glands, and in about one-third of cases there is bilateral involvement. In females the pararectal group of glands is involved most commonly. There is little pain, though some discomfort with slight fever may be noticed. The skin over the inguinal glands becomes red; the glands become matted together, and eventually a fluctuant area forms. Several sinuses may form, and from them a thick yellowish-white mucopus exudes. If a fluctuant area is aspirated the pus is found to be bacteriologically sterile; but after sinuses have formed secondary infection is usual.

In females the suppurative process may result in fistulæ between the vagina, rectum, or other pelvic viscera. Fibrosis may result in rectal stricture the symptoms of which may cause the woman to seek medical advice. In severe cases of progressive ulceration in the rectovaginal septum a cloaca may be formed. The condition is then named esthiomène.

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Schistosomiasis

The majority of human infections by the trematodes known as blood flukes are caused by *Schistosoma hæmatobium*, *S. mansoni*, and *S. japonicum*. The disease may be acquired by contact with water containing infective forms (cercariæ) of these flukes.

Such infections occur in those parts of the world where the appropriate snail intermediate hosts of the parasites are found, and where sanitation is defective or non-existent. The cycle of development of these trematodes depends upon the contamination of fresh water, in which the snails live, by fæces or urine containing live schistosoma ova. Humans form the main source of such infected excreta though mice and some domestic animals may harbour *S. japonicum*.

S. hæmatobium infection is found in large areas of Africa, especially but not exclusively in the great river basins; in Arabia and some Middle East countries; and in Madagascar and Mauritius. *S. mansoni* infection occurs in more limited foci within the areas of distribution of *S. hæmatobium* in Africa; and in Brazil, Venezuela, and some of the West Indies. *S. japonicum* infections are found in the Yangtze River basin of China, and in foci in Japan and the Philippines.

The later manifestations of infection by these flukes are due to the presence of the adults in the radicals of the vesical plexus, and the portal vein, and to the inflammatory reaction to the presence of ova in the walls of the viscera drained by these veins. It has been shown by Gelfand and Ross (1953) that ova may be widely distributed in the abdominal viscera and sometimes in other sites, such as the central nervous system, though in general *S. hæmatobium* causes vesical schistosomiasis, while *S. mansoni* and *S. japonicum* cause intestinal schistosomiasis. Hepato-splenomegaly due to fibrosis surrounding ova in these organs occurs in both types of disease, though the grosser degrees of cirrhosis resulting in portal hypertension occur in the intestinal form.

In vesical schistosomiasis the ova are found in various pelvic organs; the bladder, seminal vesicles, prostate and urethra, and in the uterus and vagina. Around the ova is a cellular reaction of lymphocytes, eosinophils and giant cells Later fibrosis causes thickening of the walls of the viscera. In heavily infected patients schistosomal granulomata *may grow on the external genitalia, and fistulæ may form in the perineum* or between pelvic viscera. Moreover, chronic pelvic peritonitis may result from this infection. Surgical treatment is needed sometimes for these complications. The help of the surgeon also may be required in diagnosis, for cystoscopy may reveal small greyish or yellowish bilharzial tubercles in the trigone of the bladder or, at a later stage, "sandy patches" which are areas of erosion of the vesical mucosa with deposition of ova and calcium salts in the submucosa. Papillomata may form. Where stenosis of the ureters with hydronephrosis has occurred ascending bacterial infection is common, and calculi may form in the urinary tract. In cases of chronic contracted bladder plastic operations to increase the bladder capacity have been attempted (Honey and Gelfand, 1956). Carcinoma of the bladder is a late complication of vesical schistosomiasis

The pathology of intestinal schistosomiasis is similar to that of the bladder infection, but ulceration, fibrosis, and papillomata develop in the large intestine so that the symptoms are those of chronic dysentery. At sigmoidoscopy ulcers or papillomata may be seen, and scrapings, or a biopsy of tissue may be taken to search for ova.

The confirmation of the diagnosis depends upon finding the ova which are characteristic in appearance: *S. hæmatobium* has oval terminal-spined eggs, *S. mansoni* has similar eggs each of which has a lateral spine, and *S. japonicum* ova are more nearly circular in outline and each has only a small rounded knob on the side. These ova are seen under the low-power microscope. Details of medical treatments, the most effective of which is

by the intravenous administration of sodium antimony tartrate, must be obtained from books on tropical medicine.

HYDATID DISEASE

Echinococcus granulosus is a small tapeworm, 3–8 mm. in length, found in the intestine of dogs, wolves, and other carnivorous animals. Ova in the fæces of the animal contaminate grass or other vegetation, which is eaten by herbivorous animals; sheep, cattle, and hogs. The embryo liberated from the ovum by the digestive juices penetrates the intestinal wall and is carried to the liver, other organs, or skeletal muscle where it is found as a cyst. From the internal cell layer of the cyst, scolices, or the heads with hooklets of developing tapeworms, are formed. When the sheep dies or is killed dogs and similar animals eating the offal or carcase ingest these scolices which, attaching themselves to the intestinal mucosa, develop into adult worms. Thus the domestication of sheep and dogs implies the possibility of this disease in man who may replace the sheep as the intermediate host of the cyst stage of the parasite. Hydatid disease is the name given to the occurrence of one or more cysts in humans, and it is commonest in sheep and cattle rearing areas especially in Australia, New Zealand, parts of South Africa, Argentina and Uruguay.

Man acquires the infection by swallowing live ova, commonly as the result of contamination of the hands by dog fæces, but possibly also from contamined grass or vegetable matter introduced into the mouth. As in the sheep the embryo liberated from the ingested ovum passes to the liver, the commonest site of a hydatid cyst, or to other organs or tissues.

The cyst has three layers in most cases. The inner two of these are part of the parasite, while the outer one is a fibrous tissue reaction on the part of the host. The innermost layer is a nucleated protoplasmic matrix from which bud-like invaginations into the cavity of the cyst are formed. These are known as brood capsules, and in them are formed the scolices each carrying two rows of hooklets and four suckers. Daughter cysts may form from these brood capsules, or by evagination of the wall of the original cyst, but new cysts may develop in other organs or tissues if any scolices are liberated from within the cyst. Inside the cyst is a clear watery fluid containing about 0·5 per cent sodium chloride and no albumin. A deposit, known as hydatid sand, is composed of free scolices and hooklets.

The middle layer is a thick, laminated elastic layer the edge of which curls up and retracts when it is incised.

The outer layer is composed of fibrous tissue. In long-standing cases calcium salts may be deposited in it, and then the cyst outline is very distinct on radiographic examination.

Rarely there is no effective encapsulation and repeated evaginations of the cyst wall produce numerous daughter cysts so that the appearances are like a bunch of grapes. Spread of scolices to other organs is much commoner in this form of multilocular or alveolar hydatid.

The hydatid cyst is a space-occupying lesion and symptoms and signs are due to pressure in the organ where it is situated. Thus, in some sites the cyst may reach a considerable size before its presence is supected. Sometimes secondary infection of the cyst occurs when the manifestations of an abscess will be present in addition. Occasionally

rupture of a cyst results in severe anaphylactoid symptoms. As has been mentioned the cyst, especially if calcified, may be demonstrated radiologically.

Investigations in a suspected case should include a leucocyte total and differential count which may show eosinophilia; a skin sensitivity test (Casoni test) in which antigen prepared from hydatid fluid, which formerly contained many scolices, is injected intradermally and, if positive, produces a wheal with erythema in about 20 minutes; and a

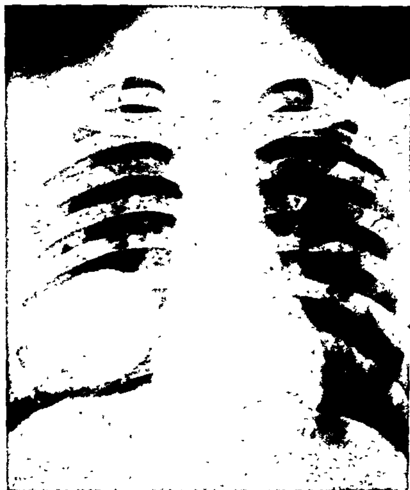


FIG 130 Radiograph of chest showing Hydatid Cyst (*Mr. R. Barrett, F R C S*)

complement fixation test on the serum of the patient. A review of results with the skin test and complement fixation test is recorded by Benstead and Atkinson (1953). Radiography may reveal the site and number of cysts.

Exploratory aspiration of a suspected hydatid cyst is dangerous, for, though the finding of a fluid of 0·5 per cent salt content with little or no protein supports the diagnosis, and though the identification of scolices or hooklets in the deposit from the fluid confirms the diagnosis, the leakage of fluid into the tissues may result in severe anaphylactic shock, and the escape of live scolices will implant cysts in other sites.

Surgical operation is the only means of eradicating cysts, and its success largely depends upon the site and number of the cysts. The aim should be to remove the cyst

intact. Where there is obvious danger of rupture of the cyst during operation part of its contents may be aspirated and replaced by 10 per cent formalin solution. After allowing 5–10 minutes for this to destroy scolices, the fluid may be withdrawn and the operation continued. When a cyst cannot be removed it may be possible to attach the margins of the skin incision to its wall. After the formation of granulations which seal off the wound margins the cyst may be punctured and drained to the exterior. This process is named marsupialization. Later the cyst wall becomes fibrosed and contracted, and may be excised safely.

LEPROSY

Leprosy, or Hansen's disease, is a chronic granulomatous condition caused by infection with *Mycobacterium lepræ*, an acid-fast organism of which the mode of spread is not yet elucidated though entry of the organism is probably through the skin. Infection probably occurs most readily in children living in close contact with a patient whose lesions contain many organisms. It is now believed that the organisms first establish themselves and multiply in the terminal nerve twigs of the skin. The resistance of the patient is an important factor in determining the clinical type of disease. On the one hand are patients having little resistance in whom rapid multiplication of the bacteria occurs and many granulomatous lesions appear in the skin. These patients do not react to an intradermal injection of Lepromin; an extract from leprosy granulomata. This is a characteristic of the lepromatous form of the disease. On the other hand are patients having considerable resistance, in whom organisms are scanty, and in whom the peripheral nerve trunks are early involved. These patients react to the intradermal injection of Lepromin. This type of the disease is named tuberculoid leprosy. Between these two extremes are many patients the classification of whose disease is a matter for the expert leprologist, and many names have been used to describe this group: intermediate, atypical, dimorphous, etc.

In those parts of the world where leprosy is common the development of an adequate leprosy service within the public health service results in the detection of early cases, and in the development of an informed and co-operative community which will encourage sufferers to accept treatment. Persistent medical treatment with sulphone compounds such as diamino-diphenyl-sulphone (D.D.S.), will cure many cases of tuberculoid leprosy and will arrest, if not cure, the disease in lepromatous leprosy. Ancillary therapeutic services, such as physiotherapy and occupational therapy are important to maintain the morale of the patients, and to prevent the deformities so often associated with advanced leprosy. The patients must be taught and encouraged to compensate for the analgesia of hands and feet and to take a pride in avoiding traumatic ulcers. Active co-operation in muscle exercises, especially for the small muscles of the hands, is most necessary.

The help of the surgeon may be required for dealing with severe, intractable nerve pain, especially in patients with tuberculoid leprosy; for the correction of deformities of hands or feet; and for the management of chronic ulcers on the feet. It is of the greatest importance that the skin area where a surgical incision is to be made should be freed from bacteria. Brand (1956) from a wide experience of surgery in patients with leprosy points out that wound healing may be delayed if the patient is malnourished; and it may be delayed if the part is insensitive and is therefore subjected to movement and minor trauma. Nerve pain, commonly in the distribution of the ulnar or peroneal nerves, may

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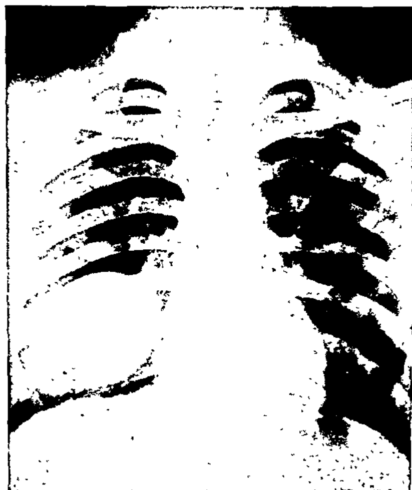


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Surgery has no place in the treatment of yaws, but the clinical manifestations may provide problems in differential diagnosis.

PRIMARY STAGE. The primary or "mother" yaw is a rounded, raised papillomatous lesion, the surface of which is yellow due to dried exudate, and the diameter of which is from 2–5 cm. It may occur anywhere on the body but is commonest on a site below the waist. It may be established on the site of a pre-existing ulcer or abrasion, in which case



FIG 131 Primary Yaw (*Dr A Zahra*)

a scar remains when it heals. A mother may acquire a primary yaw on the nipple when feeding her infant who has secondary yaws. The primary yaw heals naturally in about 6 weeks.

SECONDARY STAGE. There are skin lesions and periosteal lesions. Usually before the primary yaw has completely healed the eruption of secondary yaws appears, characterized by papillomatous lesions each like the primary yaw but smaller in size: from 5 mm. to 2 cm. in diameter. These may be numerous or scanty, being less obvious at higher altitudes and in colder climates, and tending to be more numerous in those parts of the body which perspire most. The secondary yaws eruption may occur in crops over a prolonged time, and there may be months, or even years, of clinical latency before a further eruption occurs. These lesions together with the primary yaw are the most

be due to œdema of the nerve. Or it may be due to fibrosis whether inside the nerve sheath constricting the fibres, or outside the nerve binding it down to surrounding structures. A skin incision is made not directly over the thickened nerve, and the nerve is then exposed and examined. In many cases it will be found to be irregularly thickened and pink in colour. Incision through the sheath longitudinally results in an outflow of tissue fluid, and sometimes visible shrinkage of the nerve. The skin wound may then be closed. In other cases the nerve is adherent and the dense fibrous tissue must be incised. Stripping the nerve sheath over an area of the nerve will release pressure on nerve fibres, and is often successful in relieving pain (Gramberg, 1955).

With regard to increasing the mobility of deformed hands, Brand (1952) recommended a plan consisting of measures to improve the patient's general health and to heal minor abrasions or sores on the affected part, followed by physiotherapy and exercises to mobilize the joints as far as possible, and then a transplantation of tendons. For details of operative technique his published work should be consulted.

Most chronic ulcers due to trophic disturbance in leprosy will heal if simple antiseptic measures are applied together with complete rest of the part. Prolonged confinement to bed, however, is very undesirable in this disease both because it lowers the patient's morale, and because it may result in loss of movements and power which are retained by exercise. However, a carefully shaped and fitted walking plaster will allow most of the ulcers to heal. Sometimes excision of fibrous tissue around the ulcer margin is necessary, and allows healthy granulation tissue to form.

YAWS

Yaws is due to infection by *Treponema pertenue* and occurs in hot and humid areas of the tropics among people who wear little clothing and who live in squalid conditions. Infection, probably due to direct contact between an infective lesion and the skin of the uninfected, though possibly also due to the mechanical transfer of infective material by wound-feeding flies, is commonest in childhood. The disease may persist in various forms for the remainder of the patient's life, and an important feature is the possibility of clinical latency, when the only evidence of disease is positive serological tests for syphilis. The similarity of yaws and syphilis has led some to the view that they are one disease in which the age of acquiring infection and differences of climate and environment are responsible for the clinical differences. Yaws does not affect vital organs as syphilis does, nor is there evidence that it is transmitted congenitally.

Diagnosis usually depends upon recognition of the lesions, and is supported by the discovery of treponemata, morphologically identical with *Treponema pallidum*, in serous exudate from the lesions, and by positive serological tests for syphilis.

The early lesions of yaws respond rapidly to treatment with penicillin. The World Health Organization has supported mass treatment campaigns for treponemal diseases in various countries. Patients having obvious lesions are given a single intramuscular injection of Procaine penicillin with aluminium monostearate (P.A.M.) 1·2 million units. All domestic contacts of the patient, even though apparently healthy, are given a single injection of half this amount. A further survey of the same population is made 3–6 months later and any active cases and their contacts are treated as before. These campaigns have proved very successful when forming part of a general improvement in living conditions (Troupin *et al.*, 1953).

well to anti-treponemal treatment. A thin tissue-paper type of scar remains after healing.

Occasionally irregular depigmentation, especially on the hands and feet, occurs in tertiary yaws. Possibly a form of hyperkeratosis of the palms and soles is one manifestation of this stage of the disease.

Osteitis with sequestration and sinus formation may occur. This may appear as a



FIG 133 Juxta-articular Nodes of late Yaws (*Dr A Zahra.*)

single suppurative dactylitis. A common site for osteitis in this disease is the frontal bone; and the same destructive process may affect the nasal septum and the palate. When the nose has been destroyed the resulting condition is named Gangosa.

Patients are seen with tenosynovitis on the dorsal aspects of the wrists. If such swellings are opened surgically granulation tissue will be found to be present as well as an increased amount of synovial fluid. It is wise to try the effect of a course of penicillin before undertaking surgery for ganglion in an endemic area of yaws. Painless recurrent hydrarthrosis of the knee joints may occur as a manifestation of tertiary yaws. A further unusual manifestation is the presence of juxta-articular nodes, which are nodules of dense

infective lesions. A special form of secondary yaws is known as Crab yaws. A secondary lesion forms in the sole of the foot, but is long in appearing on the surface because of the thick plantar skin. The patient limps about on the heel or the side of his foot to relieve pressure on the tender area.

Other skin manifestations are hyperkeratosis of the palms and soles. On the feet this is often accompanied by deep fissures at the margins. These are more troublesome



Fig 132 Multiple dactylitis of secondary yaws. (*Dr A Zahra*)

in the rainy seasons. Penicillin treatment for yaws, and local measures to prevent secondary infection and to relieve pressure will cure the fissures.

Periostitis occurs on the shafts of long bones, such as the ulna, radius, tibia and fibula, and it may affect a number of phalanges of the fingers: a multiple dactylitis. A similar inflammation affects the nasal processes of the maxillæ. Periostitis may resolve completely, though sometimes new bone is formed which does not disappear. Thus occurs the curious deformity of the face named Goundou.

Tertiary Stage. In this stage of the disease the skin and subcutaneous tissues, bones, and synovial membranes may be affected. A swelling may form in the subcutaneous tissue, commonly on the leg, and this eventually ulcerates. The gummatous ulcer so formed has irregular granulations in the floor and a raised rolled margin. Differentiation from chronic ulcers due to other causes is not easy, but the tertiary yaws ulcer responds

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This must be released for half a minute every 20 minutes. Failure to follow this rule has resulted in gangrene and the loss of a limb, and is one of the dangers of first aid treatment by ill-informed helpers. The tourniquet should be used till other local measures and the administration of antivenin have been accomplished. If some hours have elapsed since the patient was bitten there is no point in using a tourniquet. Where a bite is on the trunk complete excision of the area is all that is possible, but the prognosis in such bites is bad. Muscular action assists the diffusion and absorption of venom, and therefore immobilization of the part is wise.

Where possible suction should be applied to the punctures. Venoms are destroyed by gastric juice, but absorption is possible through abrasions in the mouth, and therefore it is safer to use suction-cups, if they are available, or to place thin rubber sheeting over the wound before suction is applied by the mouth. Some favour the making of small incisions to enlarge the fang punctures, and to allow a better flow of blood. Others hold the view that incisions assist the absorption of venom.

The active substances in snake venoms are neurotoxic (colubrine) and hæmotoxic (viperine). Certain snakes produce more of one substance than of the other. Neurotoxic venom acts after absorption on the medullary centres. Hæmotoxic venom acts on the vascular epithelium both locally, and generally. Thus, where the punctures are insignificant but general signs such as drowsiness, inability to walk, and difficulty with speech and swallowing are marked it is likely that neurotoxic venom has been absorbed. Where the punctures continue to ooze blood, and the part is swollen and discoloured, with œdema and discoloration gradually extending up the limb, it is likely that the venom was mainly hæmotoxic. Later, in such cases, hæmorrhage may occur from the respiratory, alimentary, or renal tracts. A decision about the type of venom may be important in the use of antivenin.

In various parts of the world medical research institutes, or larger public health laboratories can supply antivenins prepared against snake venoms common in their territory. Ideally the type of snake should be identified and the specific antivenin given in large doses by injection around the wounds, and intramuscularly above the tourniquet. Children require comparatively larger doses than adults. The actual dosage depends upon the type of antivenin, and the information provided with it by the manufacturers must be used as a guide. When antivenin has been given the tourniquet may be released, but replaced again if signs of general absorption of venom supervene.

Usually specific antivenin is not available, or the snake is not identified. Then a decision must be made as to whether a hæmotoxic or a neurotoxic antivenin is needed; and often a polyvalent antivenin must be used in hope that it will have some detoxicating action on the venom present. Intravenous administration of antivenin may be dangerous because of producing anaphylactic shock. Cortisone has proved of value in overcoming this reaction; but in some cases desensitization by small graduated doses of antivenin is necessary.

Especially in cases where hæmotoxic venom has been injected repeated blood transfusions may prove life-saving.

Wherever possible the snake which bites should be killed and brought for identification. The head is necessary for this purpose, so that the arrangement of the fangs may be examined. Detailed works on venomous snakes should be consulted for the criteria used in identification.

fibrous tissue forming near joints, particularly the knee or elbow. They may be excised if they are troublesome, and it will be found that they arise from the tendinous expansions at the attachment of the joint capsule.

Notes on the Treatment of Snake Bite

It should be generally known that most snakes will attempt to escape from humans but that they will bite if irritated or cornered. They are nocturnal in habit. Therefore the wearing of boots and leggings, or even long trousers when walking at night, and the carrying of a lamp and a stick will prove useful means of preventing snake-bite. Most bites are on the feet and legs.

People fear snakes and therefore though bitten by non-venomous species, or only imagining that they have been bitten, many show signs of severe shock. This must be treated according to general principles. All snakes have bacteria in their mouths, sometimes including anærobic organisms, and therefore every bite must be treated as a potentially infected punctured, or lacerated wound.

The site of the bite must be washed and disinfected, which will remove any venom remaining on the skin. It must be carefully inspected. Non-venomous snakes have a row of maxillary teeth, and some centrally placed palatine teeth, all of similar size. Thus a row of teeth marks of this kind is reassuring that the snake was not venomous. Venomous snakes have enlarged, grooved, or canalized teeth, usually one on each side of the maxilla in addition to small maxillary teeth. The large teeth are the fangs by which venom is injected, and they produce puncture marks if the bite was efficient. Evasive action by the patient, or the presence of clothing may have prevented a deep puncture. When distinct the fang marks are usually ½–1 in. apart, the greater distance indicating the bigger snake, and therefore potentially the greater amount of venom injected.

If the patient has just been bitten a tourniquet should be applied to cut off the circulation through the bitten area.

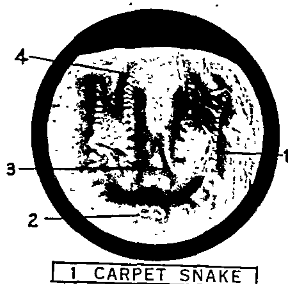




Fig 134 Dental impressions of snakes

1. Carpet snake non-venomous
   1, 2 Maxillary teeth impressions.
   3, 4: Palatine and Pterygoid teeth impressions
2. Copper-head Snake venomous
   5. Fang puncture
   6. Few maxillary teeth impressions. (*Sir N H Fairley*)

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Where possible suction should be applied to the punctures. Venoms are destroyed by gastric juice, but absorption is possible through abrasions in the mouth, and therefore it is safer to use suction-cups, if they are available, or to place thin rubber sheeting over the wound before suction is applied by the mouth. Some favour the making of small incisions to enlarge the fang punctures, and to allow a better flow of blood. Others hold the view that incisions assist the absorption of venom.

The active substances in snake venoms are neurotoxic (colubrine) and hæmotoxic (viperine). Certain snakes produce more of one substance than of the other. Neurotoxic venom acts after absorption on the medullary centres. Hæmotoxic venom acts on the vascular epithelium both locally, and generally. Thus, where the punctures are insignificant but general signs such as drowsiness, inability to walk, and difficulty with speech and swallowing are marked it is likely that neurotoxic venom has been absorbed. Where the punctures continue to ooze blood, and the part is swollen and discoloured, with œdema and discoloration gradually extending up the limb, it is likely that the venom was mainly hæmotoxic. Later, in such cases, hæmorrhage may occur from the respiratory, alimentary, or renal tracts. A decision about the type of venom may be important in the use of antivenin.

In various parts of the world medical research institutes, or larger public health laboratories can supply antivenins prepared against snake venoms common in their territory. Ideally the type of snake should be identified and the specific antivenin given in large doses by injection around the wounds, and intramuscularly above the tourniquet. Children require comparatively larger doses than adults. The actual dosage depends upon the type of antivenin, and the information provided with it by the manufacturers must be used as a guide. When antivenin has been given the tourniquet may be released, but replaced again if signs of general absorption of venom supervene.

Usually specific antivenin is not available, or the snake is not identified. Then a decision must be made as to whether a hæmotoxic or a neurotoxic antivenin is needed; and often a polyvalent antivenin must be used in hope that it will have some detoxicating action on the venom present. Intravenous administration of antivenin may be dangerous because of producing anaphylactic shock. Cortisone has proved of value in overcoming this reaction; but in some cases desensitization by small graduated doses of antivenin is necessary.

Especially in cases where hæmotoxic venom has been injected repeated blood transfusions may prove life-saving.

Wherever possible the snake which bites should be killed and brought for identification. The head is necessary for this purpose, so that the arrangement of the fangs may be examined. Detailed works on venomous snakes should be consulted for the criteria used in identification.

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CHAPTER VII

VENEREAL AND ALLIED DISEASES

G. O. HORNE

INTRODUCTION

THE term "venereal diseases" is applied to those diseases which are transmitted almost exclusively by sexual intercourse. Traditionally they are *syphilis, gonorrhœa, chancroid, lymphogranuloma inguinale* (*l. venereum*) and *granuloma inguinale* (*g. venereum*). The diseases known as "treponematoses" (*yaws, bejel, pinta,* etc.) are usually linked with the venereal diseases because of their similarity in many respects to syphilis, although their transmission is seldom attributable to sexual intercourse. *Urethritis* in the male due to causes other than the gonococcus is not conventionally a venereal disease, but it is nearly always related to sexual intercourse, though not necessarily of a promiscuous nature. *Reiter's syndrome* is a disease closely associated with "abacterial" urethritis.

Other diseases affecting the external genitals, though not always transmitted by coitus, include *balanitis, herpes genitalis, ano-genital warts,* and *moniliasis,* and can be conveniently considered in this chapter.

INCIDENCE OF VENEREAL DISEASES

There has been a great reduction in the incidence of syphilis and gonorrhœa all over the world since the immediate post-war years. In Great Britain early syphilis is now a relatively rare disease, although its later manifestations are of course more common, and will persist for many years; gonorrhœa is still relatively common but its incidence in the male is now exceeded in some areas by that of non-gonococcal urethritis.

Chancroid, lymphogranuloma inguinale and granuloma inguinale very rarely occur in Great Britain. Cases are occasionally encountered in seaports; the later manifestations of lymphogranuloma inguinale (e.g. rectal stricture) may be encountered in people who have previously lived in the tropics. The treponematoses may be encountered in natives of the tropics resident in this country.

IMPLICATIONS OF VENEREAL DISEASES

Venereal diseases have several obvious public health implications, and, although in Great Britain compulsory notification is not required, all clinics undertaking the treatment of these diseases submit returns to the central health authorities. The discovery of a case of venereal disease, at any stage in its natural history, not only has important medical, social, psychological and possibly economic implications to the patient, but also involves the tracing, investigation, and (if necessary) treatment of all others possibly infected. Although most current methods of treatment are relatively simple, responsibility for the investigation and treatment of such patients should be undertaken only by those who are aware of all the implications of the disease, and who have the necessary

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IMPLICATIONS OF VENEREAL DISEASES

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experience and facilities. This is one of the reasons why patients with venereal diseases are usually investigated and treated in special departments.

Nevertheless, on many occasions the diagnosis of venereal disease, or at least the appreciation of the necessity for investigations from this point of view, is the responsibility of others than specialists in the subject. Surgeons are liable to encounter the genito-urinary manifestations of various venereal diseases, and also some of the later manifestations of syphilis. The decreasing incidence of such diseases tends to result in their being forgotten in differential diagnosis, sometimes with unfortunate sequelæ.

SYPHILIS

Syphilis is caused by the spirochæte *Treponema pallidum*, which can be identified microscopically by the dark ground illumination method. It is usually between 7 and 12 μ in length, and consists of from 6–20 spirals. It moves slowly and purposefully across the field (in contrast to the active lashing movements of many other spirochætes with which it may be confused), the movements having three components: opening and closing of the coils, rotation on its own axis, and angulation. It has little resistance to drying and heat, and moisture is required for its human transmission.

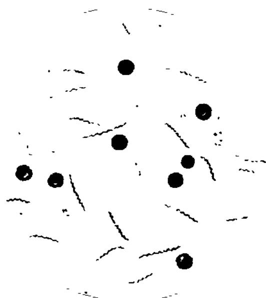


FIG. 135 Treponema pallidum.
(*From "Textbook of Venereal Disease," R R Willcox*)

At all stages of the disease the fundamental pathological lesion is an obliterative endarteritis. In the earlier lesions induration is prominent, in the later lesions, necrosis; healing results in the formation of fibrous tissue. In some of the later lesions, especially in the central nervous system, degeneration of tissues may accompany the inflammation.

Natural History of Syphilis

Syphilis is conventionally divided into several "stages," but these merely represent episodes in the life history of an exquisitely chronic disease. The variations in the manifestations of syphilis which occur among different races, between the sexes, and among individuals, may be partly due to different strains of the causative organism, but they are more probably due to variations in the host reaction. The early stages of the disease are characterized by a large number of circulating organisms and by widespread but relatively innocuous tissue reaction; the later stages, by an insignificant number of organisms and by selective, but relatively serious tissue reaction. Increased sensitivity of some tissues to the organism presumably develops over the years, and indeed, in many of the later manifestations no organisms can be found, and in a few of them specific therapy has little or no effect on the tissue reaction.

Acquired Syphilis. For the transmission of the spirochæte intimate body contact is necessary, though obvious abrasion of the skin or mucous membrane is not. Coitus

provides the ideal conditions for transmission, though this can also occur in other circumstances, such as kissing. It can (rarely) occur as a result of indirect contact through contamination of communal articles such as cups.

The incubation period is commonly 2–3 weeks, but it ranges from 1–12 weeks. At the end of this time the *primary chancre* appears at the site of inoculation (nearly always the external genitals) and is usually accompanied by enlargement of the regional lymphatic glands. Although the tissue reaction is localized the organism is already widely disseminated.

In the absence of adequate treatment the *secondary stage* follows, commonly 3–4 weeks (but occasionally up to several months) after the appearance of the chancre. The widespread tissue reaction reveals itself most commonly as skin and mucous membrane eruptions and diffuse lymphadenitis. Sometimes there is malaise, loss of weight, anorexia, and mild fever. Rarer manifestations include jaundice, iritis and meningitis. There is wide variation in the combination and prominence of these different manifestations. *T. pallidum* can be found in large numbers in moist lesions on the surface of the body. Serological tests usually do not become positive until the chancre has been present for several weeks, but are always positive at the onset of the secondary stage. Examination of the cerebrospinal fluid commonly reveals asymptomatic involvement of the central nervous system.

In the absence of adequate treatment at this stage all these lesions may clear up spontaneously, and the disease passes into the *latent stage*. This may take many months to occur, and not uncommonly there are minor exacerbations of the local lesions before the disease becomes completely latent. When there are no active lesions left on the skin and mucous membranes contagiousness ceases, although transplacental infection can still occur. A scar may mark the site of the chancre. By *latent syphilis* is meant that stage of the disease in which there is no clinical or radiological evidence of activity, and the cerebrospinal fluid (C.S.F.) is normal. If the C.S.F. shows evidence of involvement the name *asymptomatic neurosyphilis* is applied; such cases are liable to develop active neurosyphilis at a later date.

In the absence of adequate treatment in the latent stage one of three things may occur: there is a spontaneous cure; latency persists indefinitely; or the tertiary stage develops, commonly 10–15 years after infection has occurred, but sometimes earlier and sometimes much later than this. The *tertiary stage* manifests itself in three principal ways: as gummatous or fibrous lesions ("benign" tertiary syphilis); as involvement of the cardiovascular system (principally the aorta); and as involvement of the central nervous system ("meningo-vascular" or "parenchymatous"). These last two frequently occur together.

In the rare event of infection occurring as a result of direct inoculation into the blood (*syphilis d'emblée*), as at blood transfusion, the disease takes the same course, but there is no chancre and the first manifestations are those of the secondary stage.

The course of the disease, including the incubation period, and particularly the timing and prominence of the clinical manifestations, may be modified by various factors. The disease tends on the whole to pursue a less serious course in the female, and pregnancy notoriously suppresses (often completely) the early manifestations. Local application of penicillin to early lesions may result in temporary healing, but not in cure of the disease. Subcurative amounts of specific treatment, depending on the time at which it is given,

may prolong the incubation period, may temporarily suppress the early manifestations, or may result in the development of "precocious" tertiary manifestations (gummatous-like lesions of a particularly extensive and destructive type appearing within a few months or a few years of infection).

Adequate treatment may completely cure, or may only arrest the progress of the disease (with or without return to normal of serological tests and C.S.F. changes), depending principally on the time at which it is given. The likelihood of serological tests being reversed after treatment tends to lessen the longer the infection has been present. Treatment may have little beneficial effect once important tissue degeneration has occurred in the tertiary stage. Adequate treatment prevents transmission of the infection to other people and to the fœtus.

Congenital Syphilis. Syphilis can be transmitted from an infected woman to the fœtus via the placenta. Infection does not occur until the fourth month of intra-uterine life or later. The effect on the fœtus tends to diminish the longer the mother has had the disease, but transmission is possible for from 10–12 years, although eventually healthy children may be born. The fœtus may be killed *in utero* and a miscarriage, with a macerated fœtus, result; there may be a live birth, but prematurely, and the infant shows gross manifestations of infection; there may be a normal birth, and the infant develops manifestations after a few days or a few weeks; there may be a normal birth, and, although the child has syphilis, no manifestations appear until later in life.

The natural history of the congenital disease is similar to that of the acquired, the early infantile manifestations corresponding to, and being similar to, the secondary stage of the latter. These early manifestations may be absent; if present, and the infant survives, they may clear up spontaneously, and, after a latent phase, the stage corresponding to the tertiary stage of the adult may develop. This commonly occurs about puberty, i.e. 10–15 years after infection has occurred. Gummatous lesions or neurological syndromes may develop, but the cardiovascular system is rarely, if ever, affected. More common are interstitial keratitis, nerve deafness and painless effusions into joints.

Treatment has an effect on the course of congenital syphilis similar to that of the acquired disease. Syphilis is rarely, if ever, passed on to the third generation.

Principal Features of Acquired Syphilis

Primary Stage

The *primary chancre* presents in a wide variety of forms. The classical Hunterian chancre (a solitary, painless, indolent, indurated ulcer with a regular, clear margin and a clean "raw ham" base) is relatively rare, and in the genital region any erosion or ulceration, solitary or multiple, primary syphilis must be included in the differential diagnosis. There may be brawny œdema of the tissues around a primary chancre. Confusion may arise particularly with herpes genitalis, erosive balanitis, chancroid, tuberculosis, and carcinoma. In the male a genital chancre usually occurs on the glans, prepuce or frænum, or in the coronal sulcus; occasionally, inside the urethra or elsewhere about the genital region. In the female the chancre may be on the cervix (and so easily missed), on the labia, the fourchette, clitoris, or surrounding skin; rarely, in the vagina.

Extra-genital chancres may occur anywhere on the body, but most commonly about the mouth (especially the lips), anus, and fingers. On the lip the induration leads to characteristic eversion of the lip, and there may be considerable crusting of the lesion.

An anal chancre can occur in the male or female, and usually develops in the region of the external ring. It may be confused with an anal fissure, but is characteristically larger, much less painful, and accompanied by enlargement of inguinal glands. The diagnosis of extra-genital chancre is rarely made before the secondary signs have appeared.

Lymphadenitis nearly always accompanies the primary chancre, following a few days after its appearance. The regional lymph glands (usually, therefore, the inguinal glands) become moderately enlarged, are firm, discrete, and painless, and do not suppurate.

Secondary Stage

The *skin rashes* (syphilides) of secondary syphilis also present in a variety of ways, but have several characteristics: they tend to be symmetrical and widespread in distribution, are more prominent on the flexor surfaces and may involve the palms and soles;



Fig 136 Condylomata lata

they are often pleomorphic; they tend to be dull red or coppery in colour; they do not cause irritation; individual lesions may be slightly indurated. The rash is commonly macular or papular, or a combination of these two, and the papules may be scaly; occasionally the rash is pustular or proliferative. Leucodermic patches may appear on the neck, especially in women, consisting of pale macules on a pigmented background.

may prolong the incubation period, may temporarily suppress the early manifestations, or may result in the development of "precocious" tertiary manifestations (gummatous-like lesions of a particularly extensive and destructive type appearing within a few months or a few years of infection).

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reaction are slight. There may be local swelling, especially if soft tissues are involved as well. Periostitis occurs alone or along with osteitis; it is commonest in long bones; X-ray may show changes ranging from slight elevation of the periosteum to extensive and irregular formation of new subperiosteal bone. Osteitis is characterized by both new bone formation (especially in long bones) and by bone destruction (especially in flat bones such as the skull and palate, when perforation may occur). In osteomyelitis there is X-ray evidence of involvement of the bone marrow but sinus formation is unusual. Bone and joint changes also occur in neurosyphilis.

Nearly all the *viscera* in the body can be affected by gummatous or fibrotic lesions, though such lesions are very rare. (The nervous and cardiovascular systems are dealt with separately.) The disease may present as predominantly ulceration (as in the larynx and stomach); as predominantly fibrosis (as in the lungs, œsophagus, stomach, and liver), with various sequelæ; or as a hidden gumma (as in the brain, liver, mediastinum, and testicle), sometimes with obstructive sequelæ. The diagnosis of some of these lesions is frequently made only at post-mortem, but the possibility of syphilis as a cause of a multitude of conditions should always be borne in mind, and serological tests used whenever indicated.

CARDIOVASCULAR SYPHILIS. The first part of the aorta is the site most commonly affected. This may result in (*a*) dilatation of the aorta (uncomplicated aortitis; or aneurysm, fusiform or sacculated); (*b*) aortic incompetence; (*c*) coronary ischæmia. These three may occur in any combination; aortic incompetence is not commonly associated with an aneurysm, and when these occur together the possibility of a healed dissecting aneurysm should be borne in mind. Death results from heart failure or from rupture of an aneurysm.

From the surgical point of view aneurysm is the most important of these lesions. Aneurysms are most common in the ascending and transverse aorta, but may occur in the descending aorta, and rarely in the abdominal aorta. The other great arteries, such as the inominate, are occasionally affected, and, of the smaller arteries, the popliteal is most commonly affected. Operative treatment may be indicated principally to relieve pressure symptoms or to prevent further expansion and rupture of the aneurysm.

Cardiovascular syphilis commonly occurs along with neurosyphilis.

NEUROSYPHILIS. In the central nervous system the disease may principally affect the arteries and meninges (*meningo-vascular* or *cerebrospinal syphilis*) or the nerve cells and axones (*parenchymatous neurosyphilis*); gummata may occur anywhere in the brain or spinal cord, when they commonly present as space occupying lesions; neurological syndromes may result from involvement of bone (gummatous or neuropathic) in proximity to neurological structures. Neurosyphilis commonly occurs along with cardiovascular syphilis.

In *meningo-vascular syphilis* one of several types of syndromes may present, depending on the site of the lesion. They include gummatous basal meningitis (when involvement of the ocular nerves is a common feature); cerebral endarteritis (resulting in different types of palsies, including classical hemiplegia); meningo-myelitis (with characteristic signs of a transverse lesion of the cord); spinal endarteritis (with evidence of local or diffuse spinal softening); hypertrophic pachymeningitis, particularly of the cervical region (when there is evidence of compression of spinal roots and sometimes of the pyramidal tracts).

Papular lesions in areas where there is moisture and friction (especially the ano-genital region) may become abraded (*moist papules*), or they may become flattened, hypertrophied, confluent and macerated (*condylomata lata*), and exude heavily infected serum. Condylomata lata in the anal region may be confused with external hæmorrhoids, and with condylomata acuminata.

Mucous membrane lesions (*mucous patches*) occur in the mouth and throat, and, occasionally, the ano-genital region. They are small slightly raised erosions of the mucous membrane, either with a bright red appearance, or covered by a white or grey-white membrane. They are characteristically transient and painless.

Generalized lymphadenitis is a common feature of secondary syphilis. The groups involved include the posterior cervical, occipital, axillary, and epitrochlear. The glands are moderately enlarged, firm, discrete, and painless. *Alopecia* may result from syphilides on the scalp, when the hair has a typical "moth-eaten" appearance, with ill-defined and incompletely denuded patches; or it may be "neurogenic" in origin, with uniform thinning of the hair or completely denuded patches. Other, rarer, manifestations of secondary syphilis include *irido-cyclitis*, *hepatitis*, and *meningitis*.

Tertiary Stage

Gummatous and fibrous lesions may involve the skin, mucous membranes and subcutaneous tissues, bones, and viscera. *Skin and subcutaneous tissues* are usually involved together. The lesions are characteristically few in number, of asymmetrical distribution, but commonly grouped; they are indurated, indolent, and symptomless. They commonly start as nodular lesions in the skin, and may or may not ulcerate; the lesions tend to link up, forming a polycyclic outline which frequently has a hyperpigmented border; as they spread peripherally there may be spontaneous central healing, with typical atrophic "tissue paper" scarring; ultimately the lesions may heal completely.

A solitary gummatous ulcer shows several characteristic features. Its development may be precipitated by trauma; common sites include the upper part of the lower leg, the face, scalp, and buttocks; it is deep and has a punched-out appearance, with a "wash-leather" base. There may be involvement of the underlying bone. When it occurs on the lower leg it may be associated with gravitational ulceration.

Mucous membranes may be similarly involved, but the lesions are usually more destructive. The tonsillar region, naso-pharynx, the palate and the nasal septum are common sites, and, perforation of the palate and septum may occur. The *tongue* may be the site of a solitary gumma, but more commonly there is chronic glossitis, superficial or interstitial (or both): there may be red, glazed areas on the tongue (commonly painful), and the tongue may be fissured and distorted (*see* page 224, Vol. II). Leukoplakia may occur alone or along with glossitis, but is very rare in the female. The patches may be present on the inner aspects of the lips and cheeks and on the palate as well as on the tongue Leukoplakia is potentially malignant, especially when associated with fissuring of the tongue (*see* page 218, Vol. II).

Bone involvement in tertiary syphilis has several characteristic features. It may be precipitated by trauma. The bones most frequently involved are the skull, long bones of the leg and bones of the shoulder girdle, but no bone is exempt; joints are rarely involved. Pain may be marked, especially at night, but disability and constitutional

Trauma is not a necessary precipitating factor, and the onset may occur during a period of rest in bed. Changes in the joint include proliferation and destruction of cartilage, capsule, and bony surfaces, with a variable degree of new bone formation, pieces of which may become detached. Gross disorganization of the joint may ensue, but is not always accompanied by a similar degree of disability, and function may be surprisingly well preserved.

Neurotropic osteopathy. There may be localized or generalized osteoporosis with increased fragility, resulting in fractures from minimum trauma or even spontaneously.

Perforating ulcers (mal perforans) occur nearly always on the sole of the foot (commonly over the head of the first metatarsal) or on the ball of the big toe plate. They may be single or multiple. In the early stage they may simulate a large corn, and "paring" may precipitate ulceration. They are oval or circular, and deep, sometimes extending down to the bone or joint. They commonly become secondarily infected. X-ray may show involvement of underlying bone, and sequestra may be extruded. They are commonly accompanied by other neuropathic lesions.



FIG. 138 Perforating ulcer in tabes.
(From "Textbook of Venereal Disease," R R Willcox)

Bladder dysfunction may be the presenting feature of tabes dorsalis. In the early stages there may only be difficulty in initiating or completing micturition, but as the atony of the bladder develops urination becomes less frequent, the bladder distends and eventually there is overflow incontinence. Urinary infection is an almost inevitable sequel. In such cases there is always other evidence of tabes dorsalis.

Principal Features of Congenital Syphilis

INFANTILE MANIFESTATIONS

The infant may be marasmic and toxic. Skin eruptions similar to those of secondary syphilis in the adult may be present, with, in addition, bullous lesions on the palms and soles (syphilitic pemphigus). Snuffles (a purulent, sometimes bloodstained, nasal discharge), fissured and ulcerative lesions around the nose and mouth, mucous patches and condylomata lata may occur. The abdomen is frequently distended on account of enlargement of the liver and spleen. Chondroepiphysitis reveals itself as swellings, commonly in the region of the wrists and knees, and the affected limbs may appear to be paralysed (Parrot's pseudo-paralysis). X-ray reveals characteristic changes, including irregular thickening of the distal end of the metaphysis and decalcification of the

The syndromes resulting from *parenchymatous neurosyphilis* are general paralysis of the insane (when there is degeneration of the ganglion cells of the cerebral cortex and of the associated fibres and pyramidal tracts) and tabes dorsalis (when there is degeneration of the posterior nerve roots and posterior columns). Combinations of these two syndromes are frequently found—taboparesis. Optic atrophy, which is usually bilateral, may accompany either of these syndromes (more commonly tabes dorsalis), or may occur alone.

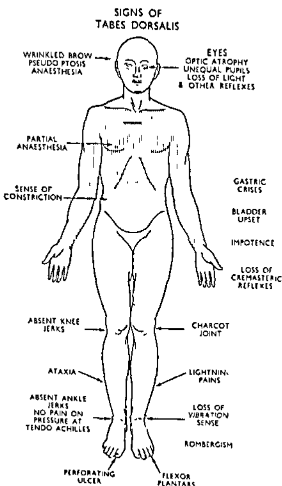


FIG 137 Signs of tabes
(From "Textbook of Venereal Disease," R R Willcox)

General paralysis of the insane (G.P.I.) is characterized by mental changes and progressive spastic paralysis. The syndrome presents in a wide range of ways, with variable proportions of these two principal elements. Pupillary abnormalities of the Argyll Robertson type are nearly always present. The syndrome sometimes presents as "congestive attacks"—short focal, or generalized convulsive attacks sometimes associated with transient aphasia or limb palsies. It has no particular surgical implications.

Tabes dorsalis is characterized by "lightning" pains in the limbs (nearly always the legs, and frequently mistaken for "rheumatism") and other paræsthesias; areflexia and hypotonia; sensory ataxia, revealed most obviously in the gait; and disturbances of micturition. The syndrome presents in a wide range of ways. Argyll Robertson pupils are nearly always present. Rare features in the later stages of the disease include visceral crises and neuropathic lesions (trophic ulcers, Charcot joints, and osteoporosis). The disease has several particular surgical implications.

Gastric crisis is the commonest visceral crisis, and usually presents with sudden onset of severe upper abdominal pain associated with intractable vomiting. One or other of these two features may predominate or occur alone. It may be mistaken for an abdominal emergency and result in unnecessary laparotomy. In a gastric crisis there may be skin hyperalgesia but rigidity is absent A gastric crisis never occurs without unequivocal historical and/or clinical evidence of tabes dorsalis, and very rarely without Argyll Robertson pupils. A tabetic patient may, of course, develop an abdominal surgical emergency. Other crises include rectal (when there is severe tenesmus), bladder (severe strangury) and laryngeal (severe laryngeal spasm).

Neurotropic arthropathy (Charcot joints). The joints most frequently involved are the knee, hip, ankle, and shoulder; vertebræ are occasionally involved, and their collapse may lead to root and spinal cord compression syndromes. The onset is commonly sudden, with a large effusion into the joint, which is usually painless but may be painful initially.

sensitivity to penicillin. Iodides are still occasionally used, but it is unlikely that they have any effect that cannot be achieved by penicillin. They are occasionally of value as a therapeutic test in possible gummatous lesions.

Penicillin

Long-acting preparations of penicillin (procaine salts suspended in water or oil, with or without aluminium monostearate; and benzathine penicillin preparations) allow effective outpatient treatment. There is no reason to believe that the higher concentrations in the blood obtained by crystalline penicillin are more effective, though preparations containing both types of penicillin are commonly used. The effectiveness of penicillin depends on both the total dosage and the time over which it is given. If the requirements in these respects are known the appropriate schedule of the selected preparation can be used, injections being given daily, or at longer intervals, as indicated.

Bismuth

Bismuth is used as a suspension of either the metal or a salt (such as oxychloride). The dose is 0·2–0·4 g., depending on body weight, and is given by deep intramuscular injection. Courses of from 10–12 weekly injections are used, with intervals of 4–6 weeks between courses. Care must be taken to avoid toxic effects (principally albuminuria, gingivitis, and dermatitis).

Treatment Reactions

These include *therapeutic shock* (Herxheimer reaction) and *therapeutic paradox*. Penicillin may cause a temporary exacerbation of local syphilitic processes a few hours after the first injection, and this may be accompanied by a sharp febrile reaction. This is of little importance in early syphilis, unless there is laryngeal involvement, when temporary œdema may lead to obstruction. It is of greater importance in neurosyphilis, especially in G.P.I., and of doubtful importance in cardiovascular syphilis, when coronary occlusion or rupture of an aneurysm could theoretically occur. If it is considered essential to avoid a Herxheimer reaction, bismuth can be given for several weeks before penicillin is started, but this is nowadays considered to be rarely necessary, except in some cases of G.P.I. If there is too rapid healing of certain lesions, fibrosis may cause undesirable results—e.g. constriction of tissues about the throat, obstructive liver disease, and compression of spinal nerve roots. The risk of this therapeutic paradox can be reduced by preparatory treatment with bismuth.

Response to Treatment

Adequate treatment with penicillin in the early stages of the disease can achieve complete cure, as shown by the permanent disappearance of all clinical manifestations and permanent seroreversal. In the later stages of latency (after the infection has been present for several years) cure can be achieved in the sense that clinical manifestations never develop subsequently but the serological tests may or may not be reversed. In the tertiary stage cure can sometimes be achieved in the sense that gummatous lesions heal and do not recur; but in neurosyphilis and cardiovascular syphilis, whilst complete cure is occasionally achieved, more frequently the disease may only be arrested, or may progress in spite of even the most vigorous treatment.

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What has been said about the diagnosis of the later stages of acquired syphilis applies also to congenital syphilis. It should be borne in mind particularly that the "scars" of congenital syphilis (such as nasal and dental deformities) persist for life, even after adequate treatment and reversal of positive blood tests. In older people with latent syphilis it may be difficult to be certain whether the infection is acquired or congenital; investigation of relatives may help.

Serological Tests

Both complement fixation tests (such as the Wassermann reaction) and flocculation tests (such as the Kahn test and the Price precipitation test) are used in the diagnosis of syphilis. Ideally a quantitative estimation should be made in one of the tests. At least 5 ml. of clotted venous blood is required for the satisfactory performance of these tests. Laboratories differ in their methods of reporting the results of such tests, and specialist advice should be sought on the interpretation of reports that are not unequivocally negative or positive.

The standard serological tests for syphilis are biological tests and so are more frail and liable to error than the more straightforward chemical and biochemical tests. They are not entirely specific for syphilis, but simply indicate the presence of a "reagin" associated with the serum globulin. This reagin may be present in conditions other than syphilis and so give temporary or permanent "biological false positive" results, although these are usually only of low titres. These conditions include pregnancy; some acute infections such as virus pneumonia, infective hepatitis and infectious mononucleosis; disseminated lupus erythematosus; malaria and leprosy; and following vaccination and inoculation. They are, of course, frequently positive in high titres in other treponemal diseases.

The more recently introduced treponema pallidum immobilization (T.P.I.) test of Nelson demonstrates the presence of a true syphilitic antibody in the blood. The test is elaborate and expensive but, whilst its role is not yet finally assessed, it is of undoubted value in interpreting equivocal results obtained from routine tests, especially in pregnancy.

Cerebrospinal Fluid

In the diagnosis of syphilis the following investigations on the C.S.F. are informative: cell count (including proportion of lymphocytes and leucocytes); total protein; globulin (whether present in excess); Wassermann reaction (including a "fractional" test, if possible); Lange curve.

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For various unavoidable reasons, some of which have already been explained, the treatment of syphilis unfortunately rests partly on an empirical basis. There is still not unanimity of opinion as to the optimum methods of treatment, and, in any event, different types of cases, and even individual cases, require separate consideration. The discussion here is confined mainly to general principles.

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GONORRHŒA

[Gonorrhœa in the male is described in the section "Urethritis in the Male." This has been done partly to economize in space, but also to draw attention to the fact that a patient presenting with a urethral discharge should be investigated as a case of "urethritis"; in Great Britain at the present time only about half of such patients will have gonorrhœa.]

By definition gonorrhœa is an inflammation of the genital and lower urinary tract, usually resulting in a purulent discharge, caused by infection with *Neisseria gonorrhœa*. The disease may spread locally, but the organism can also independently attack the rectum and conjunctiva. Infection of the skin, with abscess formation, has been reported. Invasion of the blood stream can occur, and the organism has been grown from the fluid from inflamed joints.

Bacteriology

The gonococcus is briefly defined as a Gram-negative, intracellular diplococcus, but it is morphologically indistinguishable from *N. meningitidis*, *N. catarrhalis*, and *N. sicca*, all of which can cause a similar infection. The gonococcus is a delicate organism and can be successfully cultured only if the correct technique is used. The important factors include the prompt inoculation of the uncontaminated material on to a warmed plate of correctly made chocolate agar medium, which is immediately put into an incubator. The final identification of the organism involves the use of the oxidase reaction and of sugar fermentation tests. Many strains of the gonococcus are resistant to sulphonamide, but there is no evidence of resistance to penicillin. The organism is highly sensitive to streptomycin and the broad-spectrum antibiotics.

Antibodies develop in the blood, and this is the basis of the *gonococcal complement fixation test* (G.C.F.T.) This test is rarely positive until the infection has been present for several weeks, and so is of little value in diagnosis in the early stage of the disease. Once positive, it may remain so for very long periods (sometimes for life) even after adequate treatment. The test is not entirely specific for gonorrhœa, and is sometimes positive in low titres in the absence of any current or previous gonococcal infection. It is therefore of limited value and great care is required in its interpretation.

Pathology

The incubation period is commonly 2–5 days, occasionally up to several weeks. Susceptible mucous membranes and glands are those lined by columnar and cuboidal epithelium. Sites most commonly affected are the urethra, rectum, and conjunctiva in both sexes, and the cervical canal of the uterus. The vagina is susceptible only up to the age of puberty, when the lining cells change to the resistant stratified squamous type. Gonococci can penetrate into submucous tissues. Following infection epithelial cells are shed, and there is outpouring of plasma and leucocytes. Glands and crypts are most severely involved; abscess formation may follow. The inflammatory reaction may subside with no residual lesion, or fibrous tissue in varying amounts may be formed. Some organisms may become trapped in occluded ducts and reach the surface only intermittently; threads of muco-pus may be extruded from residually infected glands. The tendency for the organism to invade glands and crypts in the mucous membrane

and ataxia, are occasionally dramatically relieved, but sometimes are completely uninfluenced; neuropathic lesions are uninfluenced. In cardiovascular syphilis anginal symptoms are frequently considerably relieved, and there is evidence that life is prolonged.

It is again emphasized that the serological tests are of limited value in assessing the results of treatment in late syphilis.

Schedules of Treatment

In primary and secondary syphilis the commonly recommended schedule of penicillin is 6 million units given over a period of about 10 days (i.e. 600,000 units procaine penicillin daily). To this can be added a course (10–12 weekly injections) of bismuth. In all the later stages a larger course—10–12 million units over 2–3 weeks—should be given, with or without 1 or 2 courses of bismuth. Some cases of late syphilis benefit from further courses of penicillin, but each case must be assessed separately. Additional forms of treatment must be given as indicated (see later).

Observation after Treatment

In early syphilis cases must be observed long enough after treatment to ascertain that there is no clinical relapse and that serological tests are reversed and remain negative. *It is customary to do blood tests 3-monthly in the first year, and 6-monthly in the second* year after treatment, and to examine the C.S.F. towards the end of this time. If all the tests are negative at the end of 2 years cure can be safely assumed.

In late latent syphilis, since serological tests may never be reversed, it is difficult to know how long observation should be maintained, but it is often against the interest of the patient to prolong this beyond a few years. Observation need not be prolonged after the healing of gummatous lesions, but patients with cardiovascular and neurosyphilis usually require indefinite observation.

Ancillary Treatment

Artificial fever (administered by inoculation with benign tertian malaria, intravenous injection of foreign protein material, or by electrical methods) still has a part to play in selected cases of neurosyphilis Topical cortisone is imperative in the treatment of interstitial keratitis. Cardiac failure requires treatment along the usual lines. In tabes dorsalis with bladder involvement urinary infection may have to be controlled.

Surgical treatment includes plastic operation (keratoplasty after interstitial keratitis with extensive scarring; reconstruction of the nose after gummatous destruction; and dental prosthesis after destruction of the palate); orthopædic appliances, arthrodesis or amputation for Charcot joints; in aneurysm of the aorta, decompression of the mediastinum or surgical attack on the aorta (measures to encourage clotting, wrapping of the aneurysm in cellophane, or excision); and in tabes dorsalis with bladder involvement, temporary or permanent cystotomy.

Congenital Syphilis

The same principles apply to the treatment of congenital syphilis. The customary dosage of penicillin in the infantile stage is 200,000 units per 1 lb. body weight, given over 10–14 days. In older children adult doses can safely be given.

Urethritis in the Male
(Including Gonorrhœa)

Mode of Infection. Infection nearly always reaches the urethra from the external meatus; it may rarely develop as a sequel of urethral stricture, of prostatic infection or of cystitis. In severe cystitis the purulent urine may leak into the urethra and, if it reaches the external meatus, may simulate a urethritis.

Causes. In Great Britain at the present time the gonococcus is responsible for about only half of the cases of urethritis. Most of the non-gonococcal infections are "abacterial," i.e. no organisms can be seen in stained smears of the urethral discharge, and no growth obtained on routine culture. No organism has yet been isolated in this type of urethritis, but evidence suggests it is virus-like in nature. Whilst the infection is nearly always related to intercourse this need not necessarily be of a promiscuous nature, and it sometimes appears to be contracted from a regular consort, and even a wife, who may show no evidence of genito-urinary disease.

The nature of "abacterial" urethritis (sometimes called "non-specific" urethritis) is not fully understood. Differentiation from gonococcal urethritis can be made only by bacteriological examination, although there are a few characteristic clinical distinguishing features: for example, the incubation period is commonly 2–3 weeks, in contrast to the 2–5 days of gonorrhœa. A gonococcal and an "abacterial" infection may be acquired coincidentally.

Other pyogenic organisms, such as *Escherichia coli* and staphylococci may rarely cause urethritis. *Trich. vaginalis* is sometimes found in urethral discharges, but it is not certain to what extent this organism is the actual cause of urethritis. Urethritis may rarely be caused by local trauma or the application of antiseptics, by prophylactics or contraceptives. Care must be taken not to mistake an increase in the normal secretions (urethrorrhœa and prostatorrhœa) for a urethritis.

Symptoms and Course of the Disease. The symptoms of urethritis include urethral irritation and pain (aggravated on erection), discharge, dysuria, increased frequency and urgency of micturition and (rarely) hæmaturia; systemic symptoms are uncommon. The extent and severity of these symptoms vary according to circumstances. If the posterior urethra is involved urgent dysuria and frequency may be marked. The profuseness and consistency and colour of the discharge may vary according to the nature of the infection: in gonorrhœa it tends to be more abundant and more purulent and yellow, and in "abacterial" urethritis less abundant, more watery, and whiter, but this difference is not constant. Whilst at least some of these symptoms are usually prominent, they may be minimal, and disease may be present and (at least in the case of gonorrhœa) capable of transmission without any symptoms whatsoever.

In the absence of adequate treatment spontaneous cure may occur, the symptomless carrier state develop (at least in the case of gonorrhœa) or complications ensue. These are rare but occur more often in gonococcal infection. Spread to the posterior urethra may be followed by involvement of the prostate gland, seminal vesicles and epididymides. There are commonly accompanying mild systemic symptoms, with some fever. With prostatitis the patients may have a sense of fullness in the rectum and perineal region, and dysuria and severe frequency are common, sometimes with terminal hæmaturia. The infection may be unilateral or bilateral. A prostatic abscess may develop.

be done a few days after treatment has been given, and again immediately after the end of the succeeding menstrual period—a time when any residual organisms are most likely to reappear. Thorough bacteriological tests should be carried out following the treatment of complications. In all cases observation should be maintained until the possibility of a coincidental syphilitic infection has been eliminated, a final blood W.R. being done 3 months after the last exposure to the risk.

Gonococcal Vulvo-vaginitis

Various organisms may be responsible for vulvo-vaginitis in children, and the ætiology can be established only by bacteriological tests. Gonococcal vulvo-vaginitis is nowadays a rare disease.

Symptoms and Signs. Symptoms may be slight, but usually the child complains of local soreness, sometimes to the extent of being unable to walk, scalding on micturition and sometimes increased frequency. Clothes may be obviously stained. On examination the vulva is usually reddened, and may be œdematous and excoriated. There may be a profuse purulent or a slight thin watery discharge from the vagina and vulva; the rectum may also be affected.

Diagnosis. This can sometimes be made on the strength of Gram-stained smears, but cultural confirmation is always desirable, particularly in view of possible medico-legal implications. Other causes of vulvo-vaginitis include thread-worms.

Treatment. Hospitalization is usually preferable and the necessary isolation measures should be applied. Local treatment, apart from ensuring local cleanliness with warm baths, is rarely required. A course of penicillin is given lasting for about a week, the dosage depending on the age of the child. Relapse (which may be relatively symptomless) sometimes occurs, and observation should be maintained for several weeks. Smears and cultures should be repeated a few days after the completion of penicillin, and again a few weeks later.

Gonococcal Ophthalmia Neonatorum

By definition ophthalmia neonatorum is any inflammation that occurs in the eyes of an infant within 21 days of birth and that is accompanied by a discharge. It must be notified to the local Medical Officer of Health. The gonococcus is now rarely a cause of ophthalmia neonatorum in Great Britain.

The organism enters the infant's eyes during the process of birth, and infection can be prevented by correct ante-natal management of the mother, and by care at the time of delivery. The infant's eyes should be carefully wiped as soon as the head is born, but it is not now customary to instil prophylactic antiseptic drops.

The infection presents within a few days of birth, and is usually severe, with a profuse seropurulent, sometimes bloodstained, discharge, and marked œdema and chemosis. Unless it is treated promptly destructive ulceration of the cornea may ensue. The diagnosis is made by examining stained smears of the discharge, and by culture if necessary. The condition responds promptly to parenteral penicillin, but local treatment is essential during the first few hours. Frequent lavage of the eye, with saline or a weak antiseptic, should be carried out until the infection is under control. Penicillin drops (1:10.000 solution) can be instilled into the conjunctival sac.

specimen of discharge should be diluted in normal saline and immediately examined under the microscope. Special techniques are also available for detecting the parasite.

If local complications are present the prostate gland should not be massaged as a diagnostic procedure. With the onset of gonococcal epididymo-orchitis the urethral discharge may become scanty, but the organism can usually be isolated from the urine if no urethral secretion is available for examination.

Treatment

GONORRHŒA

Uncomplicated gonorrhœa can be cured in nearly every case by a single injection of procaine penicillin: 300,000 units is an effective dose, and the one commonly used. If, for any reason, penicillin is contraindicated, g.l. streptomycin is equally effective. No local treatment is required. If local complications are present rest in bed and symptomatic treatment may be required for a short period, but there is a prompt response to penicillin, which should be given in larger doses (e.g. 600,000 units procaine penicillin daily) over a period of several days, depending on the response.

Although a single dose of penicillin is almost infallible in uncomplicated cases, the patient should be seen subsequently in order to confirm cure. Elaborate bacteriological investigations are unnecessary provided that, after allowing a few days for the inflamed mucosa to return to normal, there is no urethral discharge and the urine is clear and free from threads. Examination of the prostatic fluid is usually unnecessary; it should be borne in mind that a slight excess of pus cells may persist in the fluid for a few weeks after treatment, but this is of little significance. If the urethral discharge does not clear up, or if it returns, bacteriological investigations must be repeated. If gonococci are found, larger doses of penicillin should be given; if not, the case should be treated as one of "abacterial" urethritis.

If local complications have occurred the prostatic fluid should be examined microscopically (and preferably also bacteriologically) before surveillance is completed, but several weeks should be allowed to elapse before this is done.

"ABACTERIAL" URETHRITIS

The majority of cases of "abacterial" urethritis respond well to most of the broad-spectrum antibiotics. Terramycin (g.1—2 daily for 5–7 days) will promptly cure at least 75 per cent of cases, although some of them may relapse, most of these responding again to a further course. It is important to allow adequate time for the inflamed mucosa to return to normal, and over-treatment should be avoided. A few cases are resistant, and for these urethral irrigations are used by some authorities, but here again over-treatment is to be avoided. Urethral "catarrh" may persist for many weeks after an attack of "abacterial" urethritis, and treatment should be pursued only when there is definite evidence of infection.

Particularly in resistant cases, and if complications have occurred, the prostatic fluid should be examined before the patient is declared cured.

Chronic Prostatitis

[*See also* page 106, Vol. III]

Chronic infection of the prostate is an uncommon sequel of venereal disease. It should be borne in mind, however, as a possible cause of persistent or relapsing

When the infection spreads along the vas deferens the epididymis and testis are usually involved together; the infection is usually only unilateral; the prostate may or may not be obviously involved as well. In the gonococcal type pain and swelling are usually marked, with redness and œdema of the scrotum; there may be quite a large accompanying hydrocele.

Diffusion of gonococci by the blood stream rarely occurs. It may lead to the development of purulent arthritis of one or more of the large joints, which, if untreated, may cause destruction of cartilage and subsequent ankylosis. The organism can be cultured from the infected joint fluid. It is now fairly certain that the previously so-called "metastatic" complications of gonorrhœa (polyarthritis, iritis, and keratodermia blenorrhagica) are associated with a concomitant "abacterial" infection, and are not attributable to gonococci. These manifestations are discussed under Reiter's syndrome.

Examination. It is important that sufficient clothing be removed in order to allow full access to the groin and perineum. After general inspection the genitals are carefully examined. There may be some œdema of the prepuce and lymphadenitis of the penis with local tenderness. The prepuce, if present, should be retracted if possible, any discharge wiped away, and the glans and inner surface of the prepuce inspected. Even if phimosis is present (either congenital or as a result of œdema) it is usually possible to retract the prepuce far enough to reveal the urethral meatus. It is important not to mistake a subpreputial discharge for a urethral discharge.

The meatus may be reddened and the lips pouting. The urethral orifice should be carefully cleaned with an antiseptic and a specimen of the discharge obtained with a sterilized platinum loop or swab from well inside the meatus. If there is no obvious discharge the urethra should be firmly "milked" from the perineum forwards. It is important to know when the patient last micturated, since if this was very recently, little or no discharge can be expected, and examination may be more rewarding if it is postponed. Smears and cultures are made from the material obtained. The patient then passes urine into two glasses: if only the first of the two glasses contains pus it can be assumed that the infection is confined to the anterior urethra; if both glasses contain pus the posterior urethra is probably involved as well.

The inguinal glands are palpated, and other local disease such as ulceration and warts, is sought. The scrotal contents are palpated, particularly to discover whether there is any involvement of the epididymes or testes. A rectal examination is done only if there is reason to suspect the possibility of involvement of the prostate gland and seminal vesicles (i.e. it is not indicated in a case of anterior urethritis).

A specimen of blood is taken for W.R., and for G.C.F.T. if indicated (*see* page 359).

Diagnosis. It is nearly always possible to decide whether a case of frank urethritis is gonococcal or not on the evidence of a stained slide, since the Gram-negative intracellular diplococci are easily distinguished. A slide may not reveal the organism in milder cases and in the carrier state, and in such cases (and always where there are possible medico-legal complications) cultural investigations should be made as well. A diagnosis of gonorrhœa should never be made on clinical grounds alone.

In nearly every case of urethritis not due to the gonococcus, no organisms are seen in stained slides, and no significant growth obtained on culture, provided the material has been collected carefully to avoid contamination. If *trich. vaginalis* is being sought a

specimen of discharge should be diluted in normal saline and immediately examined under the microscope. Special techniques are also available for detecting the parasite.

If local complications are present the prostate gland should not be massaged as a diagnostic procedure. With the onset of gonococcal epididymo-orchitis the urethral discharge may become scanty, but the organism can usually be isolated from the urine if no urethral secretion is available for examination.

Treatment

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are the knee, ankle, and small joints of the feet, in that order, but any other joint may also be involved. There is usually a variable degree of malaise and fever, and the blood sedimentation rate is considerably raised; some cases are very toxic and lose weight. Other manifestations include balanitis circinata (*see* page 370), frequently; iritis and keratodermia blenorrhagica (a characteristic hyperkerotatic rash affecting principally the soles of the feet) occasionally.

The arthritis subsides spontaneously in a few weeks or a few months, although arthralgia may persist for a longer period. Very seldom are there permanent changes in the joints, except the feet, where calcaneal spurs, deformities, and persistent pain may call for orthopædic treatment.

Treatment. It is difficult to assess the value of specific treatment, but a large course (1–2 weeks) of a broad-spectrum antibiotic such as terramycin should always be given at the onset, especially if urethritis is present. Conjunctival and urethral irrigations are rarely necessary. Affected joints should be rested, but movements should be maintained, and the joints should not be immobilized in plaster. Analgesics can be used to control pain. Cortisone and ACTH will suppress the joint manifestations but are rarely indicated; it is unlikely that they alter the course of the disease significantly. Topical and/or parenteral cortisone should always be used for the control of iritis.

CHANCROID

(Ulcus molle, soft chancre, soft sore)

This relatively rare venereal disease is caused by the *Hæmophilus ducreyi*, and is characterized by painful genital ulceration and bubo formation. After a short incubation period (usually 3–7 days) the typical ulcer develops: it is painful, necrotic, bleeds easily and is not indurated. Several such ulcers may be present. There is usually inguinal adenitis, and in the typical chancroidal "bubo" the painful enlarged glands fuse, suppurate, and may rupture through the skin.

The organism can be isolated from the ulcer, but only with difficulty. A more or less specific intradermal reaction (Ito-Reenstierna test) can be used in diagnosis, but is not positive until several weeks after infection; also, it may remain positive indefinitely even after treatment. The diagnosis is usually made by the history and clinical appearances, and after the elimination of syphilis by dark-ground microscopy. Syphilis and chancroid may occur together.

Sulphonamides (such as sulphathiazole) are very effective in treatment, and most lesions heal with a course of 4 g. daily for 5–7 days. Streptomycin (1 g. daily for 5–7 days) and the broad-spectrum antibiotics are also effective. Penicillin is of little value. If the bubo fluctuates it should be aspirated rather than incised.

LYMPHOGRANULOMA INGUINALE

(Lymphogranuloma venereum, climatic bubo)

This chronic contagious disease is caused by a virus of the psittocosis group. It is characterized by a small fleeting primary lesion on the external genitals, which appears after an incubation period of from 5–21 days, followed by the development of regional adenitis, which is usually suppurative. Inguinal adenitis develops a few weeks, but sometimes up to a few months, after exposure to infection, and may be unilateral or

urethritis. Its role as a "septic focus" related to distant conditions (such as iritis) is a doubtful one.

A diagnosis of chronic prostatitis cannot be made simply by digital examination of the gland. It must be massaged, and microscopic examination made of the fluid itself and of the urine passed immediately after the examination. The fluid should be cultured if there is reason to suspect a gonococcal infection.

The interpretation of the findings in the prostatic fluid is difficult. More than about ten polymorphs per one-twelfth inch objective field makes infection likely, but the more cells present (and especially if they are clumped) the more certain the diagnosis. Treatment is rarely satisfactory. Broad-spectrum antibiotics can be tried. Drainage of the gland by massage once or twice weekly for several weeks is sometimes of value.

Urethral Stricture

[*See also* page 143, Vol. III]

Urethral stricture is a very rare sequel to urethritis provided cases are properly managed, and in particular if instrumentation is avoided at all stages of the disease. It should be borne in mind, however, as a possible cause of resistant or recurrent urethritis, and under such circumstances careful investigation of the urethra may be indicated.

REITER'S SYNDROME

This is a syndrome of indefinite ætiology, and about which there is still considerable controversy. It behaves in some ways like a diffuse collagen disease, although there is almost certainly an associated infective agent, so far not isolated. It is a self-limiting disease, responds little to treatment (although some of the manifestations can be suppressed by cortisone) and tends to recur. The three most constant features are abacterial conjunctivitis, abacterial urethritis, and polyarthritis. Incomplete forms of the syndrome occur, and it is probably sometimes confused with other syndromes. It may occur in both sexes as a complication of dysentery, but in Great Britain no such cases have been reported. More commonly it is related to sexual intercourse, when it occurs only in men, but it is not necessarily a "venereal" disease.



Fig. 141. Keratodermia blenorrhagica

The usual sequence at onset, spread over a few days or a few weeks, is conjunctivitis, urethritis, and then polyarthritis. The conjunctivitis is usually bilateral and may be so mild and transient as to escape notice, or severe with a purulent discharge; the urethritis varies similarly and may have to be sought carefully; polyarthritis is the predominant feature, and the joints most often affected

THE NON-VENEREAL TREPONEMATOSES

There are many diseases which occur in tropical areas, attributable to an organism almost identical to *t. pallidum*, but which are spread in a non-venereal manner, and are frequently acquired in childhood. In some of them, such as *Bejel, Pinta*, and *Njovera* many of the lesions in all stages of the disease are very similar to those of syphilis. These diseases are highly contagious in the early stages, and are easily spread non-sexually.

Yaws (frambœsia tropica, etc.) is the commonest of the non-venereal treponematoses, and is responsible for a great deal of morbidity throughout the tropics, though vigorous action by World Health Organization has recently reduced this considerably. Some of the later lesions of yaws are similar to those of tertiary syphilis, the commonest being gummatous-like ulcers, periostitis, and endosteal gummata; tenosynovitis and ganglion-like lesions also occur. Such lesions are occasionally seen in natives of the tropics in Great Britain. Serological tests give results similar to those in syphilis. The disease responds dramatically to penicillin in a dose similar to that used for syphilis, but serological tests often remain positive for many years after successful treatment.

BALANITIS

[Inflammation of the glans penis (*balanitis*) and of the inner surface of the prepuce (*posthitis*) frequently occur together, but *balanitis* is conventionally used to include *balano-posthitis*. The term is loosely applied to several conditions affecting these sites in addition to those due to true inflammation.]

Balanitis vulgaris (or *balanitis*, unqualified) is the name applied to the most common type of inflammation occurring in the uncircumcised, and attributable usually to accumulation of smegma, local irritation, and lack of cleanliness, where the organisms concerned are usually the normal inhabitants of the subpreputial sac. It is more likely to occur the greater the degree of phimosis and it may be precipitated by the irritation of a urethral discharge or urinary deposits, or by minor trauma associated with masturbation or coitus. Itching, burning or pain is complained of. There is usually a mild diffuse inflammation of the glans and prepuce, with or without superficial erosions and fissures, and a sero-purulent exudate. There may be some œdema of the prepuce and lymphangitis, aggravating any phimosis present. The inguinal glands may be slightly enlarged and tender.

It is important to ascertain whether a subpreputial discharge is urethral in origin. If the prepuce cannot at first be retracted the discharge should be examined bacteriologically to eliminate gonorrhœa; and since a primary chancre may be the underlying factor (and primary syphilis can itself present as balanitis), the secretion should also be examined for *t. pallidum* if there is any reason to suspect that the patient has been exposed to the risk of contracting syphilis

Frequent local cleansing with a weak antiseptic lotion usually clears up the condition quickly. If there is phimosis frequent subpreputial irrigations with a suitable syringe or soft rubber catheter, using saline (until syphilis has been excluded) or a weak antiseptic lotion, may be required initially In such cases the resolution is frequently hastened by a course of a sulphonamide (e.g. 4 g. daily for 5–7 days). Penicillin should be avoided

bilateral. The glands are tender and are usually considerably enlarged and matted. The overlying skin is frequently œdematous and attached to the underlying tissues, and may be purplish in colour. The femoral and iliac glands may also be involved. The glands may break down and multiple sinuses develop.

The more chronic lesions result from lymphatic obstruction which causes gross brawny œdema of the genital region (elephantiasis; "esthiomène" in the female) with or without ulceration and fistulæ. Ano-rectal involvement is much more common in the female. There is an inflammatory proctitis which, in the early stages, often presents with symptoms similar to ulcerative colitis, and polypoidal or lobulated granulomatous growths may be seen at or near the anal orifice. More usually the disease presents years later as rectal strictures of various types. In the male it is believed that the lesions of the ano-rectal region are sometimes the result of involvement of the mucous membrane following sodomy, but in the female strictures follow involvement of the intrapelvic glands.

The early stages, especially when there is marked inguinal adenopathy, are frequently accompanied by systemic upset, including fever, malaise, headache and arthralgia. The blood proteins are sometimes lowered, with reversal of the albumin-globulin ratio.

The diagnosis is made on combined clinical and laboratory investigations. The Frei test is a more or less specific intradermal test: 0·1 ml. of the antigen is injected intradermally into the flexor aspect of the forearm. If it is positive, 48 hours later there is a firm papule at least 0·5 mm. in diameter; it is usually larger, and a nodule may develop and even break down. Sometimes the reaction may not develop for several days, and so suspects should be observed for a week. A suitable commercial preparation, which includes a control injection, is *Lygranum* (Squibb). The test has several limitations. It may not become positive for several weeks after infection has occurred, and, in spite of successful treatment, may persist for variable periods after, sometimes for life. A positive Frei test means only that the patient was at some time infected with the virus of lymphogranuloma inginale, and does not necessarily mean that the lesion under investigation is due to this infection. Complement-fixation tests (dilutions of 1 in 40, or over, are significant) are of value, but positive results also persist for variable periods even after successful treatment.

In the early stages the disease responds to many of the broad-spectrum antibiotics, aureomycin having the best reputation. Artificial fever is of value in resolving the adenitis in resistant cases. The treatment of rectal strictures is dealt with on page 529 (Vol. I).

GRANULOMA INGUINALE

(Granuloma venereum)

This chronic granulomatous disease affecting the groin is attributed to *Donovania granulomatis*. It starts as a genital lesion which spreads to involve the groin and perineum. It may be predominantly exuberant (with bright red, raised, velvety granulomatous areas), ulcerative and destructive, or cicatricial (when there are areas of spontaneous healing, with scars). Very rarely are lymph glands involved. Pain is uncommon and systemic manifestations minimal. The organism can be isolated with difficulty from the lesion. The histological appearance is not specific (though it may reveal Donovan bodies), but will distinguish from malignancy. Streptomycin and many of the broad-spectrum antibiotics have been shown to be very effective in treatment.

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until syphilis has definitely been excluded. A dorsal slit is rarely necessary, and should normally not be done until the effect of local treatment and of sulphonamide has been tried.

Any important underlying cause should be sought, and, in particular, glycosuria should be excluded (it is estimated that about 7 per cent of male diabetics develop balanitis, usually due to monilial infection, and the disease may present itself in this way). Recurrent attacks of balanitis associated with phimosis may not cease until circumcision has been carried out.

Erosive balanitis (fuso-spirillary balanitis) is a more severe inflammation caused by Vincent's spirochætes and fusiform bacilli. It may be venereal in origin, but its development is encouraged by phimosis, lack of cleanliness, and minor trauma. It is characterized by grey or white necrotic lesions on the glans and prepuce; when the slough is cast off erosions with necrotic borders are left; these enlarge and may become confluent. There is accompanying profuse and foul-smelling pus. The condition is extremely painful. *Gangrenous balanitis* may ensue in some cases, the lesions becoming more extensive and turning black, with a serosanguinous discharge. In particularly virulent infections *phagedena* may develop, with rapid destructive spread, sometimes even to the abdominal wall; hæmorrhage occasionally occurs. Toxæmia is frequently present in the more severe cases.

The milder forms of this type of balanitis may clear up with simple local treatment, combined with sulphonamides, but in severe cases large doses of penicillin and/or terramycin should be used, even although the possibility of concomitant syphilis has not been eliminated Surgical treatment may be required if phimosis is present.

Balanitis xerotica obliterans is a clear-cut condition of unknown ætiology, although it is similar in many ways to kraurosis vulvæ. It is a chronic, progressive, atrophic, sclerosing process affecting principally the perimeatal region of the glans and terminal part of the urethra, and nearly always resulting in some degree of meatal stenosis. It may start acutely, with considerable exudation from the meatal region, simulating a urethritis; there may be local pain and itching; the exudate is viscid, bullæ may form, and sometimes complete occlusion of the meatus may occur, the patient presenting with urinary retention; or it may develop very slowly, the patient becoming aware over months or even years of narrowing of the urinary stream.

When the condition is fully developed the glans may appear to be somewhat shrivelled, but characteristically the skin, particularly surrounding the meatus, is thin, smooth, and shiny, and bluish-white or ivory coloured. The meatus is narrowed and may be only pin-point. The prepuce may also be involved, constriction resulting from the development of white sclerotic bands. Adhesions may develop between the prepuce and glans The condition is precancerous.

No therapy appears to have much influence on the development of the condition, though in the early exudative stage the local application of a stilbœstrol ointment (daily or more frequent inunctions) is reported to be of value. The important thing is to dilate the meatal stricture as required. There is some evidence to suggest that regular dilatation (e.g. at monthly or shorter intervals) in the early stages may have an ultimate beneficial effect.

Balanitis circinata is the name given to the characteristic lesions that develop on the glans and prepuce in Reiter's syndrome (*see* page 366). The condition begins as discrete

areas of inflammation, separated by normal skin, which tend to coalesce and form larger serpiginous and sharply defined areas, especially in the coronal sulcus and posterior part of the glans. They are exudative in the early stages, but later usually become scaly and hypertrophic.

Other conditions affecting the glans and prepuce, and sometimes confused with venereal disease, include *lichen planus*, *leukoplakia* and *erythroplasia of Queyrat* (characterized by slightly raised red shiny, smooth, velvet-like plaques); the last two are potentially malignant. Solitary ulcers of this region, which may be confused with syphilis, include those due to chancroid (*see* page 367) and to tuberculosis and malignant disease.

ANO-GENITAL WARTS

(Venereal warts; soft warts; condylomata acuminata; veruccæ acuminata)

Warts occurring in the ano-genital region are similar in some respects to those elsewhere on the body. They nearly always occur as a result of sexual contact, though their growth is encouraged by moisture, such as is provided by chronic discharges. The lesions are nearly always multiple and pedunculated, and vary in size from tiny specks to large cauliflower-like masses. On the free skin they may be pigmented and cornified, but on moist mucous surfaces they are softer and may bleed with trauma. When they are large the surface may become macerated and secondarily infected.

In the male they occur in the coronal sulcus or elsewhere on the glans and prepuce, at the urinary meatus, and occasionally inside the urethra (where they may present as slight hæmaturia). In the female they occur anywhere on the vulva, and are usually more widespread than in the male; they are frequently aggravated by pregnancy. In both sexes they occur around the anus.

Treatment must include the removal of any aggravating factor, such as a vaginal discharge or balanitis. Podophyllin is very effective in destroying warts on mucous surfaces. It is commonly used in a strength of 25 per cent in mineral oil, in compound tincture of benzoin, or in spirit. After local cleaning the preparation is carefully applied by means of an orange stick and cotton wool, ensuring that it reaches the base of the lesions, and avoiding unnecessary spread to the surrounding tissues. After it has dried it can be freely dusted with talcum powder. The podophyllin should be thoroughly washed off with soap and water about 6 hours later.

Some degree of local reaction is inevitable, especially under a tight prepuce; considerable discomfort may occur, and œdema lead to phimosis. After a day or so the warts blanch and necrosis follows a few days later. Cleanliness is necessary during this stage to avoid secondary infection, but no scarring should result. Several applications may be required, but sufficient time should be allowed between the applications for necrosis to occur. Careful planning may be necessary when there is a large crop to be dealt with in order to avoid severe reactions and repeated reinoculation. Intra-urethral warts can be dealt with similarly, using a speculum or urethroscope if necessary. Vulvar and perianal warts respond similarly, although podophyllin has little effect on warts on true skin.

As an alternative, a 3 per cent solution of podophyllin in propylene glycol can be used. This is less likely to cause a reaction, but more applications are required. An

application should be made daily (and left untouched) until the warts disappear, suspending treatment temporarily if there is any local reaction. If the warts are cornified an ointment containing 20 per cent podophyllin and 25 per cent salicylic acid, or even stronger caustics, may be necessary.

Sometimes such measures are ineffective, and occasionally the warts spread more rapidly than they can be dealt with. It is important to ensure that reinfection is not



FIG 142 Condylomata acuminata.

occurring from intra-urethral warts or from the sexual partner. When warts are extensive and involve principally the prepuce circumcision may be indicated, but this is sometimes followed by extensive inoculation of the wound. When treatment of this type fails they may have to be removed by cautery or diathermy. X-ray therapy may occasionally have to be employed, but care must be taken to avoid excessive dosage.

GENITAL HERPES

(Herpes genitalis, herpes progenitalis; herpes simplex)

Herpes genitalis may follow illicit intercourse, but is not always thus connected. It is prone to be recurrent. In the uncircumcised male the typical eruption of grouped

vesicles on an inflamed base occurs most frequently in the coronal sulcus; in the female, on any part of the vulva and rarely on the vaginal wall. Due to friction and moisture the vesicles quickly become superficial erosions. They may remain discrete or become confluent. The eruption usually causes irritation and is sometimes painful; it may become secondarily infected. There may be some local œdema, especially in the female, and the inguinal glands may be slightly enlarged and tender.

Treatment should be aimed at avoiding secondary infection, since the condition heals spontaneously, though sometimes slowly, and without scarring. It is best kept dry with the help of the application of a simple non-irritant dusting powder, but a mild antiseptic lotion or weak dye solution can be used. If secondary infection is present sulphonamides are of value, either as a powder locally or by mouth (e.g. 4 g. daily for 5–7 days). Penicillin is of little value, and should be avoided at least until syphilis has been definitely excluded. Terramycin appears occasionally to be of value.

Recurrent attacks may cause considerable distress and are sometimes difficult to interrupt. The possibility of reinfection from the same source should be eliminated; attention should be paid to the general state of health. Circumcision may have to be done. Local X-ray therapy in fractional dosage is sometimes of value. Repeated vaccination has been recommended.

GENITAL MONILIASIS

Moniliasis (thrush) of the vagina and vulva due to *Candida* (*monilia*) *albicans* is not uncommon. The same organism causes lesions of the male genitals, and can be transferred conjugally. It shows itself as balanitis (when it is commonly associated with glycosuria); as crural intertrigo (when it may simulate a tinea infection); or as a more widespread eruption affecting the penis and scrotum and perineal and anal regions (when the eruption is characteristically itchy, and frequently becomes secondarily infected, leading to œdema and sometimes painful erosions and fissures).

Treatment must include the control of any systemic contributory factor, such as glycosuria or the side-effects of antibiotics. Gentian violet (1 or 2 per cent solution) is an effective local application.

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CHAPTER VIII

RADIOLOGY AS A DIAGNOSTIC AID IN CLINICAL SURGERY

J. H. MIDDLEMISS

IT is not the intention to produce here a miniature text-book on radiology as such a work could only be inferior to standard books on the subject. Recent advances in radiology are often technical in nature and may have little application to the day to day work of the practising surgeon, and therefore lie outside the sphere of this book. The writer has principally selected his subjects from those on which his surgical colleagues have consulted him in daily practice in a busy teaching hospital. In particular an attempt has been made to emphasize the scope and limitations of radiology as a diagnostic aid. It is essential, however, for the surgeon to realize that the greatest benefit will come from frequent personal contact and consultation with the radiologist and to realize that the radiologist, by virtue of his training and experience, is best adapted to decide how to conduct a radiological examination and how to derive the maximum information from the radiological investigation of any particular clinical problem. This, however, he can only do if he is aware of the clinical problem and is not merely asked to conduct an examination as a technical feat. It should therefore be the aim of the surgeon requesting an X-ray examination to provide the radiologist with the necessary clinical details of the case to be investigated, rather than to give instructions of technical requirements and then leave him to decide how to conduct it.

EMERGENCY WORK

In any general hospital in an industrial town it is common for up to one-quarter of the total number of X-ray investigations to be emergency cases mainly referred from the casualty department. That does not imply that a quarter of the work of such an X-ray department is casualty work, for, of course, many of these investigations are of a minor nature quickly carried out Nevertheless it is an indication of the importance of the aid that X-ray facilities are required to provide in this field of medical practice. It may be argued that much of this work is of doubtful necessity or is only necessary for medico-legal purposes, and that doctors more experienced than casualty house officers would call on this service far less, yet while it is true that those experienced in such work rely more on their clinical judgement, casualty house officers must gain their clinical experience, and while doing so must have some clinical freedom. Further it must not be forgotten that in those cases where inexperienced doctors have relied on their clinical judgement, and have subsequently been proven to be wrong, the judgement of the courts has often gone hard against them if they have failed to have the patient X-rayed

In this sphere four subjects have been selected for discussion.

(1) Conditions of Skeletal Trauma that may be Missed Despite the X-ray Examination

(*a*) **Posterior Dislocation of the Shoulder Joint.** This is an unusual injury, the physical signs of which are often masked by swelling. In particular, swelling may mask the



FIG 143 A P and Vertical projection in a case of posterior dislocation of the shoulder joint

flattening of the anterior aspect of the shoulder and prominence of the coracoid process which become apparent as the swelling subsides, by which time of course valuable time has been lost in reducing the dislocation with resulting permanent disability.

Radiographically a single antero-posterior film of the shoulder may not reveal the dislocation, and in all cases of shoulder injury it should be routine practice to take a vertical projection of the joint This is most conveniently taken with the X-ray tube above the shoulder and a curved cassette in the axilla, but if the patient is unable to abduct the

shoulder a satisfactory demonstration can be achieved by putting the cassette above the shoulder and the X-ray tube below without moving the elbow from the patient's side. This projection will always demonstrate a posterior dislocation as well as bony relationships in any other form of shoulder injury.

On the routine antero-posterior film the features which suggest posterior dislocation (see Fig. 143) are:

(i) Internal rotation of the head of the humerus.

(ii) Loss of parallelism between the articular surfaces of the head of the humerus and the glenoid fossa.

(iii) The head of the humerus appearing "smaller" and its trabecular pattern more clearly defined than usual; this is due to the head of the humerus being nearer the film than normally.

(*b*) **Trans-scapho-perilunar fracture-dislocation of the Carpus.** The radiographic features of this injury may be difficult to interpret if the surgeon is not familiar with the



FIG 144 P A and Lateral projection of the wrist showing fracture of the scaphoid and dislocation of the carpus posterior to the lunate

appearances. As in all fracture-dislocations time is an essential factor in treatment, so it is of importance to recognize the nature of the injury at the first examination.

In this injury the scaphoid is fractured, the lunate and proximal half of the scaphoid are in normal relationship with the radius, and all other carpal bones including the distal half of the scaphoid are dislocated backwards.

In most hospitals the routine practice in X-raying wrist injuries is to take three projections, a postero-anterior, an oblique and a lateral. The bony injury, the scaphoid fracture and possibly an associated fracture of the radial styloid, will be readily seen on the postero-anterior film; but it is the lateral film which shows the posterior dislocation of the carpus (see Fig. 144).

(2) Head Injuries

Radiographically head injuries can be classified as fractures of the vault of skull, fractures of the base of skull, and fractures of the facial bones.

X-ray examinations of the head require, besides the co-operation of the patient, exact *and precise positioning* of the patient's head, positions some of them difficult to achieve and maintain. It is useless to send a badly shocked or concussed patient for X-ray



FIG 145 Injury to the face with considerable soft tissue swelling. The film shows fracture of the lateral wall of the left antrum and obliteration of its air-space by hæmorrhage.

examination of the head as films obtained under such conditions are unlikely to be of diagnostic value. Unless it is the surgeon's intention to deal immediately with a head injury and it is desired to demonstrate the extent of or exclude a depressed fracture of the vault, shocked or concussed patients should be treated accordingly before being sent for X-ray examination.

(*a*) **Fractures of the Vault of the Skull.** Of the three radiographic divisions the vault is the simplest to demonstrate, only antero-posterior and lateral projections being required. Fractures of the vault may be seen to be linear or stellate, to cross recognizable vascular channels such as the middle meningeal vessels, or to involve air sinuses such as the frontal sinus. Depression of a fracture will probably not be detected unless stereographic views or a special tangential projection of the fracture site is taken. Probably a

shoulder a satisfactory demonstration can be achieved by putting the cassette above the shoulder and the X-ray tube below without moving the elbow from the patient's side. This projection will always demonstrate a posterior dislocation as well as bony relationships in any other form of shoulder injury.

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showing as pools of contrast medium without recognizable calyceal structure; (e) extra-capsular rupture with contrast medium tracking outside the kidney; (f) failure to excrete or diminished excretion by the affected kidney; it is important to realize that a kidney which is functionless following injury can recover completely; (g) displacement of the kidney or displacement of the ureter by the retroperitoneal hæmatoma.

By this investigation the presence and condition of the unaffected kidney are shown. Similarly, the presence of previously unsuspected renal pathology may be shown; for instance a hydronephrotic kidney ruptures and bleeds more easily than a normal kidney. And finally when conservative treatment is being employed, the progress of the injury and its repair can be studied by serial urographic studies (see Fig. 146).

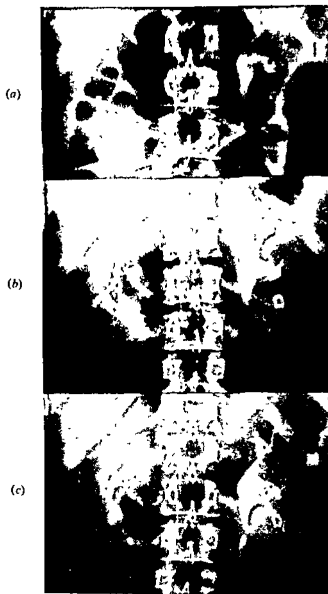


FIG 146 Excretion urography in a case of hæmaturia following injury at football (a) On the day of injury (b) Two weeks later (c) Four weeks after (b)

(a) Shows meteroism, impaired excretion by the right kidney and absence of its middle calyx
(b) Shows an intra-capsular tear with a pool of contrast medium within the renal substance
(c) Shows complete repair and normal function by the injured kidney

(4) Abdominal Emergencies

For the radiological investigation of intestinal emergencies only high quality films taken with high output machines in the X-ray Department are of any diagnostic value. Films taken with a mobile unit are rarely of the required quality and attempts to interpret them are more likely to be misleading than helpful.

(a) **Intussusception.** Intussusception in the adult is usually chronic and is usually demonstrated during barium enema investigation of alteration in bowel habit or of intermittent attacks of colicky abdominal pain.

Intussusception in childhood is commonly acute in onset, and the clinical picture is often sufficiently clear-cut to require no radiological investigation. Occasionally however there may be no palpable tumour and the surgeon may be uncertain of the diagnosis, especially as many of the clinical features of this condition may be simulated by an acute gastro-enteritis. The present low mortality in intussusception is only maintained by early surgical treatment which is dependent on early diagnosis.

more certain way of detection is examination with the surgeon's finger during toilet of the scalp.

(*b*) **Fractures of the Base of the Skull.** A fracture of the base is a diagnosis usually made on clinical grounds. Radiographic demonstration of the base of skull is a difficult manœuvre requiring the full co-operation of the patient—co-operation usually far beyond the power of any patient on whom a clinical diagnosis of fracture of the base has been made. Further, if following a clinical diagnosis of fracture of the base of skull, even the most satisfactory films fail to demonstrate a fracture line, the patient will still be treated for fracture of the base. If for academic or medico-legal purposes it is desired to have a permanent record of the fracture, the patient can safely be sent for X-ray examination the day before his discharge when he is able to co-operate fully, for such fracture lines persist for many months or even years.

(*c*) **Fractures of the Facial Bones.** These injuries comprise fractures of the nasal bones, lateral face fractures, and depressed fractures of the zygomatic arch, upper and lower middle face fractures, and fractures of the mandible. Their significance is concerned mainly with three factors—they may be concerned with alterations in vision, particularly diplopia, they may be concerned with dental occlusion and they may have cosmetic effects (see Fig. 145).

Radiographic procedure to demonstrate such fractures is again a precise technique needing considerable co-operation by the patient, and it cannot be too strongly emphasized that a shocked or concussed patient is unable to co-operate, and that in such cases when fractures of the facial bones are suspected the patient should not be sent for X-ray examination until he has been treated for shock.

(3) Kidney Injuries

A patient arriving in hospital with hæmaturia following injury to the trunk often presents a difficult surgical problem. Accurate clinical examination is rendered difficult by the marked abdominal rigidity. In such cases the injury may be severe, but it is not uncommon for hæmaturia to follow quite trivial injuries and it is an established fact that the extent of the hæmaturia bears little relationship to the severity of the kidney damage.

There is no place for retrograde pyelography in these cases. The risk of causing further hæmorrhage or introducing infection are too great, especially in an era when the emphasis is on the conservative treatment of kidney injuries.

The surgeon requires to know (*a*) the extent of the kidney damage; (*b*) that the other kidney is present and functioning normally, and (*c*) the presence of any associated injuries. All this information is readily obtainable by means of excretion (intravenous) urography which can be safely undertaken once the period of initial shock has been overcome.

The preliminary films may show the following features in cases of kidney trauma: (*a*) a slight "protective" scoliosis concave to the affected side; (*b*) obliteration of the psoas shadow; (*c*) loss of the kidney outline; (*d*) fullness of the affected flank; (*e*) injury to the bony skeleton, usually the 12th rib or upper lumbar transverse processes; (*f*) meteroism of the bowel, often very marked, frequently localized over the injured kidney.

On excretion urography the following features may be seen: (*a*) failure of visualization of a calyx; (*b*) irregularity of one or more calyces; (*c*) calyceal rupture (intracapsular) as evidenced by a pool of contrast medium contained within the kidney outline; (*d*) intra-capsular tear so extensive as to cause complete disorganization of the kidney

showing as pools of contrast medium without recognizable calyceal structure; (*e*) extra-capsular rupture with contrast medium tracking outside the kidney; (*f*) failure to excrete or diminished excretion by the affected kidney; it is important to realize that a kidney which is functionless following injury can recover completely; (*g*) displacement of the kidney or displacement of the ureter by the retroperitoneal hæmatoma.

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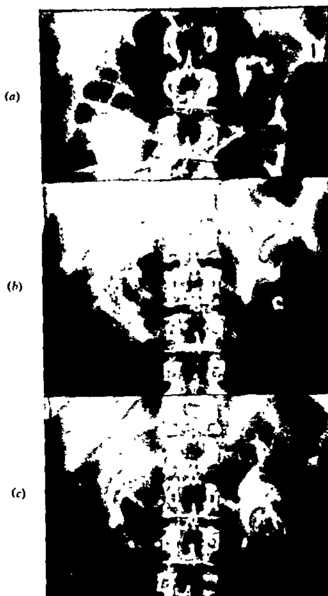


Fig 146. Excretion urography in a case of hæmaturia following injury at football (*a*) On the day of injury. (*b*) Two weeks later. (*c*) Four weeks after (*b*).

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(*c*) Shows complete repair and normal function by the injured kidney.

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In cases of doubt, plain radiography of the abdomen can help. The radiological appearances of intussusception may be:

(i) Direct visualization of the intussusception, the caput showing as a rounded convex shadow projecting into gas in the colon distal to it. Gas in the lumen in the intussusceptum may be seen as a linear shadow proximal to this (see Fig. 147).



FIG 147 Plain radiograph of the abdomen in a case of intussusception in an infant, showing the caput of the intussusceptum outlined against gas in colon distal to it

(ii) A soft tissue mass in the right lower quadrant of the abdomen, with complete absence of intestinal gas from this quadrant, and displacement of gaseously distended bowel to other segments of the abdomen

(iii) The radiological picture of intestinal obstruction without any indication of the cause.

A barium enema should rarely be necessary as a diagnostic measure.

The practice of therapeutic reduction of intussusception by barium enema, which has been widely used for many years in Scandinavia, is gaining popularity in this country. There are certainly no grounds for a change from the surgical technique which has long been accepted in this country unless equally certain and satisfactory results can be obtained by this non-operative procedure. If therefore it is to be carried out, it should

only be done by an experienced radiologist with the consent of and in the presence of the surgeon who must accept the responsibility of operating on the child if this procedure proves unsuccessful. The barium enema technique is as follows:

(i) Preliminary plain films of the abdomen are taken in order to assess the degree of intestinal obstruction and, if possible, the type of intussusception.

(ii) Barium enema is then administered under low pressure (i.e. a column of 12–18 in.) under fluoroscopic control in order to demonstrate and localize the caput of the intussusception. Films are taken at this stage.

The occlusion of the child's anus by a firm cotton-wool pad or by a metal or plastic obturator and the constant control of this by a nurse or radiographer is of great importance.



FIG 148 Supine and erect films of the abdomen of a three day old infant with signs of obstruction, showing distension of the ileum, stasis in the ileum, complete absence of gas from the large bowel and peritoneal "layering" due to peritoneal exudate. At operation atresia of the terminal ileum was found

(iii) The hydrostatic pressure is then gradually increased by increasing the height of the column of barium up to 3 or 4 feet. In exceptional cases it may be necessary to raise it to 5 ft., but usually 3 ft. is enough. Reduction is controlled by fluoroscopic observation; palpation and manipulation are not performed, reduction being entirely by hydrostatic pressure. Reduction is considered to be complete when (*a*) complete filling of the cæcum is observed and (*b*) there is flooding of the barium back into the ileum. Further films are taken at this point.

(iv) Whether or not reduction is successful the barium is drained off, and post-evacuation films taken. The whole series of films can then be studied for full evaluation of the state of affairs.

(v) If there is any doubt as to the success of the reduction, the whole procedure may be repeated.

(vi) Post barium enema care and observation are, of course, essential.

(*b*) **Perforation of a Hollow Viscus.** Perforation of a gastric or duodenal ulcer usually allows an escape of sufficient gas into the peritoneal cavity to allow its demonstration provided a horizontal X-ray beam is used. If the patient can stand the free gas will be demonstrated under the diaphragm, but if he is unfit to stand for the examination, a



FIG 149. Supine film of the abdomen in a case of volvulus of the sigmoid colon showing great distension of the single loop of colon

horizontal beam can still be used with him lying in the lateral decubitus position or even a lateral film of the abdomen with the patient supine.

Perforation of an inflamed viscus, such as the appendix or a diverticulitis of the colon, rarely allows the escape of intestinal gas. Plain radiography of the abdomen in such cases will show the appearances of an inflammatory ileus. It is not recommended that radiological aid should be a routine diagnostic measure in such cases for the diagnosis will be apparent from a proper clinical examination. Nevertheless when radiological aid is invoked in the elucidation of difficult or suspected cases of abdominal emergency, this pattern will be sometimes encountered and it is essential that those faced with the need to interpret the investigation should be familiar with its appearances, which are described on page 383 under post-operative ileus.

(*c*) **Intestinal Obstruction.** This subject has been discussed elsewhere in this textbook.

To summarize, the radiological appearances of intestinal obstruction are abnormal gaseous distension of and stasis in gut proximal to the obstructing lesion, and absence of gas from gut distal to the lesion. Stasis is shown by separation of gas and fluid to form fluid levels in the distended loops of bowel with the patient in the erect position or when some other means of using a horizontal X-ray beam is employed. It must however be realized that fluid levels alone are not an indication of obstruction; they merely mean that the contents of a particular loop of gut were static at the moment of exposure.

The usual practice is to take an antero-posterior film of the abdomen with the patient supine, and a postero-anterior film with him erect. If the patient is unfit to stand for the second film, it is sufficient to take only the former for it is usually possible to make a complete analysis of all the bowel shadows present from the supine film.

Probably the most valuable field for the application of this investigation is in cases of suspected neonatal obstruction. Swallowed air has usually reached the lower colon and rectum by 12 hours after birth and invariably by 24 hours, so that after that time a useful opinion can be given regarding the presence or not of an obstructing lesion (see Fig. 148).

In cases of doubt, surgical practice is to keep a patient under observation and to carry out clinical examination from time to time. The same procedure can and should be applied to radiological examinations, and if after a period of hours there still remains doubt, further radiological examination may be of diagnostic value. This applies particularly again to the field of neonatal problems and in suspected obstruction in childhood.

Certain special forms of obstruction have characteristic appearances which should always be borne in mind, such as meconium ileus in the neonatal period and volvulus in adults. In the former, in addition to the usual radiological signs of mechanical intestinal obstruction, there can often also be identified in the lower right quadrant of the abdomen the speckled densities of retained meconium.

In volvulus the single loop of distended bowel may be seen crossing and occupying the entire abdomen; in these cases, the distension of the twisted loop of bowel often reaches very considerable proportions (see Fig. 149).

POST-OPERATIVE CONDITIONS

(1) Post-operative Ileus

This condition may be either an inhibition ileus or an inflammatory ileus, but in practice the two may co-exist and it is often not possible to separate the one clearly from the other.

The problem that sometimes faces the surgeon is, when on the fifth or sixth post-operative day the patient begins to vomit and his abdomen becomes progressively distended, to decide whether this is an ileus or a supervening mechanical obstruction requiring further surgery. The diagnosis may be further confused by the presence of audible bowel sounds and the passage of flatus.

Radiological examination of the abdomen in these cases can often help. It must again be emphasized, however, that films taken with a ward mobile unit and under ward conditions are rarely of sufficient quality to be helpful and may even be misleading. If this examination is to be of any significance, the films must be of the very highest quality, such as can only be produced using high output apparatus and a Potter-Bucky grid in the

(vi) Post barium enema care and observation are, of course, essential.

(*b*) **Perforation of a Hollow Viscus.** Perforation of a gastric or duodenal ulcer usually allows an escape of sufficient gas into the peritoneal cavity to allow its demonstration provided a horizontal X-ray beam is used. If the patient can stand the free gas will be demonstrated under the diaphragm, but if he is unfit to stand for the examination, a horizontal beam can still be used with him lying in the lateral decubitus position or even a lateral film of the abdomen with the patient supine.



FIG 149 Supine film of the abdomen in a case of volvulus of the sigmoid colon showing great distension of the single loop of colon.

Perforation of an inflamed viscus, such as the appendix or a diverticulitis of the colon, rarely allows the escape of intestinal gas. Plain radiography of the abdomen in such cases will show the appearances of an inflammatory ileus. It is not recommended that radiological aid should be a routine diagnostic measure in such cases for the diagnosis will be apparent from a proper clinical examination. Nevertheless when radiological aid is invoked in the elucidation of difficult or suspected cases of abdominal emergency, this pattern will be sometimes encountered and it is essential that those faced with the need to interpret the investigation should be familiar with its appearances, which are described on page 383 under post-operative ileus.

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shadow that is both wider and denser than normal, due to peritoneal œdema or exudate (see Fig. 150).

It must be remembered that some degree of bowel distension occurs as a result of any laparotomy in which bowel is handled. The interpretation of these investigations is no simple matter and the differentiation on X-ray films between simple post-operative distension, post-operative ileus, and a mechanical obstruction is often a problem requiring great experience and it is wise in these cases always to have a radiological opinion.

(2) Swabs Left in the Abdomen

Despite careful precautions, routine swab counts and established techniques, there still arise unfortunate cases of swabs left in the abdomen, and there still comes the occasion in the theatre when despite counts and re-counts a swab remains missing.

Swabs, unfortunately, are not opaque to X-rays and cast no shadows.

Some commercial firms have produced swabs containing a single impregnated thread which will cast a shadow, and their use for all abdominal operations is becoming increasingly popular.

Alternatively, some surgeons have devised the practice of always clipping a Michel's clip to a swab before introducing it to the abdominal cavity. The metal clip, of course, is easily demonstrable radiologically, and in cases of doubt an X-ray mobile unit can be brought to the theatre for a film of the abdomen to be taken before the patient leaves.

(3) Sub-phrenic Abscess

The clinical diagnosis of sub-phrenic abscess is often difficult to make. Radiological investigation has a very definite rôle to play in establishing a diagnosis. Similarly in suspected cases of sub-phrenic abscess, if all the radiological criteria are absent, the surgeon can feel reasonably certain that the possibility is unlikely, though it may never be said to be positively excluded. The radiological features that may be found in this condition consist of changes in the diaphragm, changes above the diaphragm, and changes below the diaphragm.

A full examination should consist of (*a*) screen examination of the diaphragm; (*b*) postero-anterior and lateral films of the chest; (*c*) a penetrated antero-posterior film of the chest; (*d*) a postero-anterior film of the upper abdomen with the patient erect.

The changes in the diaphragm consist of:

(*a*) Diminution or absence of movement of the diaphragm on the affected side.

(*b*) Elevation of the diaphragm on the affected side.

Elevation of the dome may be either localized or generalized. It is however a difficult sign to evaluate; the right dome of the diaphragm is normally an inch higher than the left in an adult, and any variations in the normal contours may be produced either when a patient is unable to stand for the examination or unable to achieve normal respiratory excursion (see Fig. 151).

(*c*) Loss of definition of the outline of the affected dome of the diaphragm (see Fig. 152). This, too, is a difficult sign to evaluate in a patient who is perhaps unable to co-operate fully, but may be of significance when there is asymmetry between the two domes of the diaphragm and there are other confirmatory radiological signs.

X-ray department. The surgeon-in-charge therefore must decide whether the information that may be forthcoming from such an investigation is sufficiently in the interests of the patient and is likely to influence the course of treatment to such an extent as to warrant the patient's journey to the X-ray department.

Preferably two films of the abdomen should be taken, one with the patient supine,



FIG 150 Supine film of the abdomen showing an inflammatory ileus in a 12 year old boy six days after drainage for a perforated appendix.

and one erect, but if he is unable to stand, valuable diagnostic evidence can be obtained from the supine film.

In an ileus, gas is usually present to a varying degree through all the bowel, large and small. If the ileus is localized, for example in relation to a localizing pelvic abscess, then the loops of gut, both large and small, in that segment are abnormally distended and there may be local peritoneal "layering." If the ileus is generalized as in a true inhibition ileus, then the abnormal distension of multiple loops of small and large bowel occupies the whole abdomen. If the condition is a generalized inflammatory ileus, associated with a generalized peritonitis, then in addition to the widespread abnormal distension there will also be diffuse peritoneal "layering" and loss of the pro-peritoneal line. The term *peritoneal "layering"* is used to denote that loops of gut are separated by a soft tissue

The changes above the diaphragm consist of:

(*a*) Pleural effusion. This is a common event in sub-phrenic abscess. A small effusion obliterates the costo-phrenic angle, while a larger one obscures the outline of the diaphragm and rises laterally along the axillary border. Elevation of the dome of the diaphragm may render the appearances difficult to interpret, but the penetrated film of the chest will usually establish the point.

(*b*) Inflammatory lung changes. These are usually localized, being due to direct spread of the inflammatory process across the diaphragm, and have the appearance of patchy or lobular consolidation in a lung segment in direct contact with the diaphragm (*see* Fig. 151).

(*c*) Pulmonary collapse. This is not a common finding, but when it occurs it is invariably the lower lobe of a lung, and if occurring alongside some of the other changes described is confirmatory evidence.

(*d*) Suppurative lung changes. Rarely sub-phrenic abscess may give rise to an empyema or lung abscess.

The changes below the diaphragm consist of:

(*a*) An abnormal gas collection below the diaphragm. Gas following laparotomy is usually demonstrable for 5–7 days following operation, but may persist for up to 10 days. After that time, extra-intestinal gas below the diaphragm must be regarded as abnormal. However, the presence of gas in sub-phrenic abscess is a relatively rare finding, being present in fewer than a quarter of all cases.

(*b*) An extra-intestinal fluid level. This finding requires the presence of both gas and fluid, and really is a corollary to (*a*); that is to say that when gas is demonstrated, if the radiological examination is continued to that end, a fluid level will almost invariably be found.

(4) Pulmonary Infarction

In many cases of pulmonary infarction occurring as a post-operative complication, the episode and the clinical symptoms and signs leave no doubt as to the diagnosis. However, there are cases in which the symptoms and signs are less clear-cut in which it is essential to establish a definite clinical diagnosis before instituting anti-coagulant therapy.

Radiological aid can usually be of help in these cases.

The radiological signs of pulmonary infarction on a chest X-ray film (see Fig. 153) consist of:

(*a*) Diaphragmatic changes. The most common alteration is elevation of the dome of the diaphragm on the affected side; less commonly "peaking" of the diaphragm will be detectable, in which at one point the affected dome is drawn up to a sharp point.

(*b*) Pleural changes. A small localized effusion is the commonest change. Large effusions do [illegible] costo-phrenic angle. This pleural œdema or effusion actually occurs in the pleura adjacent to the segment of affected lung.

(*c*) Lung changes. In many cases there is no detectable lung shadow, while in some few massive consolidation of a whole lobe may be seen. When there is abnormal shadowing, the commonest finding is a small rounded shadow in the periphery of the lung



FIG. 151 The diaphragm in a case of sub-phrenic abscess The right dome is elevated and there are inflammatory changes in lung tissue overlying the diaphragm.



FIG. 152 Loss of definition of the right dome of the diaphragm in a case of sub-phrenic abscess.

The changes above the diaphragm consist of:

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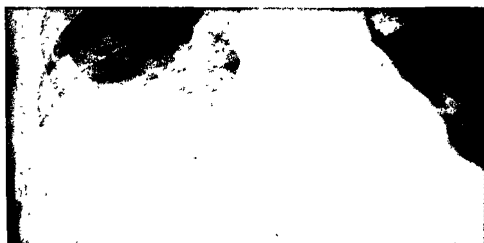


FIG 151 The diaphragm in a case of sub-phrenic abscess The right dome is elevated and there are inflammatory changes in lung tissue overlying the diaphragm



FIG. 152. Loss of definition of the right dome of the diaphragm in a case of sub-phrenic abscess

The following features may be determined from this examination:

(*a*) The condition and situation of the trachea. Often considerable tracheal compression arises in thyroid enlargement giving rise to serious respiratory embarrassment (see Fig. 154). Frontal and lateral X-ray projections of the thoracic inlet will usually demonstrate the extent of the narrowing of the trachea from this cause. If the goitre is



FIG 154. Thoracic inlet showing compression and deviation to the right of the trachea by a large goitre. There is considerable calcification both in the walls of, and within, the enlarged thyroid

nodular indentations on the anterior surface of the trachea may be seen. Similarly deviation of the trachea in this condition may be slight or marked, and its exact lateral or posterior deviation can be estimated. Sometimes a tongue of thyroid will project downwards behind the trachea displacing it forwards; the demonstration of this provides useful pre-operative information (see Fig. 155 (*b*)).

(*b*) Calcification within the thyroid. This may be due actually to calcification in the walls of an adenoma, or may occur in a hæmatoma following hæmorrhage within the thyroid. In the latter event the calcification often has a "flocculent" appearance (see Figs. 154 and 155 (*a*)).

(*c*) Retrosternal projection of the thyroid. Retrosternal thyroid may arise as an extension of a clinically recognizable cervical goitre or the tumour may be entirely intrathoracic. When there is intra-thoracic extension, the trachea is usually displaced backwards, and there may be increased prominence of the aortic knuckle due to downward displacement of the arch. Often the downward projection from the cervical swelling is diffuse and bilateral, but sometimes the intra-thoracic mass projects markedly to one side from the mediastinal border. On screen examination such a tumour can be

with clearly defined edges; it always has a pleural surface, though this may not be demonstrated unless oblique projections are taken.

If the chest film is taken within the first 24 hours after the clinical episode there may be no radiological abnormality. If the film is of first-class quality—this may not be achieved with ill patients—it may be possible to detect a segment of relative ischæmia in



FIG 153 Portable chest film in a case of pulmonary infarct. There is elevation of the right dome of the diaphragm, a small pleural effusion in the costo-phrenic angle and a considerable lung opacity adjacent to the pleural effusion

the lung, and even to see the abrupt end of a large pulmonary vessel. This is the period of ischæmia following the arrival of the embolus, when collateral vessels are attempting to maintain circulation, and before the actual onset of true infarction. A further film 24 hours later will often show this segment of lung now to consist of solid infarct.

Of the changes described, none alone is diagnostic of pulmonary infarction. Two or more occurring together, alongside the clinical picture will usually establish the diagnosis.

THYROID

Where surgery of the thyroid is being considered, it is wise to adopt the practice of X-raying the thoracic inlet and the chest as a routine pre-operative measure. Often information of use to the surgeon will be forthcoming from this procedure.

The following features may be determined from this examination:

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(a)



(b)



FIG 155 (*a*) Calcification in the thyroid lying anterior to the trachea. The soft tissue space behind the trachea is normal
(*b*) Increase in the soft tissue space behind the trachea due to projection of thyroid into that tissue plane There is also compression of the trachea.



confirmed as thyroid tissue by observing its upward movement on swallowing. Not uncommonly there may be calcification within the intra-thoracic mass.

With the advance in the treatment of carcinoma of the thyroid there are two further features which may be of clinical significance. Metastases to bone from carcinoma of the thyroid present, in about 50 per cent of cases, as solitary osteolytic bone lesions. They are usually well defined, destructive bone lesions arising in the medulla and expanding the cortex, rarely producing any periosteal or other osteo-blastic activity. They often extend into the peri-osseous tissues (see Fig. 156).

Metastases from tumours in which the radio-active iodine up-take is considerable, especially if they are in lungs, may become more radio-opaque due to their iodine content. Their progress can then be observed by serial X-ray examinations.

SALIVARY GLANDS

Recurrent or persistent swelling of a salivary gland often produces a difficult diagnostic problem. In the sub-mandibular gland the cause is usually a calculus, and less frequently a benign tumour. In the parotid gland, calculi are rare, and the more common



FIG. 157. Normal parotid sialogram

causes are (*a*) non-obstructive pyogenic parotitis; (*b*) duct stenosis or (*c*) parotitis secondary to duct stenosis. Occasionally benign or malignant tumours occur.

Radiological investigation consists of plain X-ray examination and sialography.

In the sub-mandibular gland plain X-ray examination will often reveal the calculus and there is no need to proceed further. In the case of the parotid gland in order to gain useful information it is usually necessary to carry out sialography (see Fig. 157).

(a)



(b)



FIG 155 (a) Calcification in the thyroid lying anterior to the trachea. The soft tissue space behind the trachea is normal.
(b) Increase in the soft tissue space behind the trachea due to projection of thyroid into that tissue plane There is also compression of the trachea.



FIG 156 Osteolytic metastasis with a large peri-osseous soft tissue swelling in th medial end of the right clavicle from a carcinoma of roid

The technique is to cannulate the duct and to inject an opaque medium. The simplest cannula to use is a lachrymal duct cannula. In cases of duct stenosis it is usually necessary to dilate the papilla with lachrymal duct dilators. An iodized oil (Neohydriol) is the opaque medium of choice as the water-soluble media tend to pour back round the cannula. Injection should be carried to the point where there is definite discomfort in the gland—usually ½–1 cc. is required for the sub-mandibular gland and at least 2 cc. for the parotid gland. For complete examination it is desirable to achieve acinar filling; in the past this has been wrongly termed sialo-acinar reflux and compared to pyelo-renal back-flow; it is not however a backflow phenomenon, but merely complete filling of the duct-acinar system.

Non-obstructive pyogenic parotitis, which may be due to a variety of organisms, including streptococcus viridans and the pneumococcus, manifests itself as a series of sacculæ of varying size studded along all the subsidiary ducts through the substance of the gland. It has been likened to the appearance of saccular bronchiectasis and the term sialectasis or sialangiectasis coined to denote the condition (see Fig. 158).

In either gland stenosis may be papillary or buccal, but wherever the site of the stenosis there is always dilatation of the duct proximal to the obstruction. If recurrent pyogenic infection occurs secondary to duct stenosis, in addition to the dilated main duct, beading is seen along the subsidiary ducts with probably saccule formation along and at the ends of some of them (see Fig. 159). Tumours such as tuberculous adenopathy of lymphoid tissue or "mixed" parotid tumours show as filling defects within the gland substance. The former are usually circumscribed and clearly defined, and the latter in their early stages not uncommonly produce similar appearances.

ALIMENTARY TRACT

Radiological examination of the alimentary tract in the hands of an experienced radiologist has reached a very high degree of accuracy. Nevertheless, in this sphere perhaps more than in any other, the warning note must be sounded that this is merely part of and not the whole examination of the patient. Radiological examinations are complementary to and should only follow full clinical examination. It is perhaps true to say that in this field a positive X-ray finding is usually significant but a negative result must always be accepted with reserve. Even in this age of high X-ray diagnostic accuracy there is still a place for the occasional exploratory laparatomy, and in the presence of some such positive finding as a persistent occult blood, a failure to detect an abnormality radiologically must be placed in its proper perspective alongside other clinical and laboratory data

(1) The Œsophagus

The value of radiological investigation of the œsophagus by barium examination has long been recognized, and the appearance of cardiospasm, carcinoma of the œsophagus and stricture of the œsophagus are familiar to all.

It should be realized, however, that a full radiological examination of the œsophagus entails screen examination of the patient recumbent as well as erect, and entails filling the stomach with barium in order to determine competence of the cardia and exclude hiatus hernia. When, therefore, the radiologist is asked to investigate a problem such as



FIG 158. Parotid sialogram showing diffuse sialectasis due to non-obstructive pyogenic parotitis



FIG. 159. Sub-mandibular sialogram showing papillary duct stenosis with dilatation of the main duct and of its main branches within the gland There is also a buccal stenosis of the duct

is usually demonstrable in cases of œsophagitis; and in long-standing cases in which the inflammatory changes and ulceration have caused cicatrization, stenosis of the œsophagus may be present.

(*b*) **Hiatus Hernia.** Full radiological examination will almost always reveal the presence of hiatus hernia. It may be sliding or incarcerated in type but long-standing



FIG. 160 (*b*) Hiatus hernia There is a large herniated pouch of stomach, para-œsophageal in type, but the œsophagus enters the stomach above the diaphragm

herniæ tend to become fixed, either by the development of fibrous tissue around the sac and peri-œsophageal tissues due to local inflammatory changes, or by cicatrical stenosis and shortening of the œsophagus.

The surgical treatment of the condition is influenced by the presence or not of cicatricial changes in the œsophagus. Radiological investigation of hiatus hernia, therefore, is directed not only to its diagnosis, but also to demonstrating the state of the œsophagus, its course and its point of entry into the stomach (see Fig. 160 (*b*)).

(*c*) **Œsophageal Varices.** These commonly occur in cases of portal hypertension and are best demonstrated radiologically by means of portal venography which can conveniently be carried out by percutaneous splenic injection. However, in the investigation of recurrent hæmatemesis, barium examination of the upper alimentary tract is a simpler

dysphagia, the request entails not just a "barium swallow" but "barium examination of the œsophagus."

Conditions which require some consideration are:

(*a*) **Œsophagitis.** Œsophagitis may exist without there being demonstrable or detectable radiological signs. Its presence depends on the regurgitation of acid-bearing



FIG 160 (*a*) Hiatus hernia There is spasm of the lower end of the œsophagus and an ulcer crater about two inches above the diaphragm—evidence of œsophagitis

gastric contents, and the appearances which may occur in this condition, and on which a diagnosis may be made, are:

(i) The demonstration at screen examination of free regurgitation from stomach into œsophagus; *this may sometimes have the appearance of a see-saw or to-and-fro* motion, and especially in infants the flow may go from stomach to œsophagus and back again with each respiration.

(ii) Spasm of the lower end of the œsophagus sometimes producing a serrated outline.

(iii) The presence of an actual ulcer crater in the lower end of the œsophagus due to peptic ulceration (see Fig. 160 (*a*)).

(iv) The presence of tertiary contractions throughout the œsophagus. Hiatus hernia

on every case is probably unattainable, but surgeons and radiologists should certainly meet regularly to discuss problematical cases, should devise a system of consultation over special cases and a system of advising the radiologist of the surgeon's operative findings (including the radiologist's successful diagnoses as well as his failures), for it is only by continuing to learn and by developing such conditions of mutual trust and confidence, of understanding each other's problems, that the best interests of the patient will be served.



FIG. 162. Demonstration of the elongated pyloric canal in a case of pyloric stenosis.

Four conditions with regard to radiological diagnosis of the stomach are worthy of special note

(*a*) **Congenital Hypertrophic Pyloric Stenosis.** In infants the emptying time of the stomach is very variable, up to 6–7 hours being within normal limits, while delay in commencement of emptying can be due to pylorospasm induced by the artificiality of the barium feed and the surroundings of the X-ray room. The only radiological signs that are of true value are the demonstration of the narrowed and elongated pyloric canal (see Fig. 162) and the visualization at screen examination of deep hyper-active peristaltic waves

(*b*) **Retrograde Jejuno-gastric Intussusception.** Following gastro-jejunostomy, retrograde intussusception may occur either as an acute or a chronic condition. The acute state may occur 7–10 days after operation, and is probably due to œdema round the anastomosis with a loop of jejunum becoming locked in the œdematous stoma. With continuous suction and attention to the patient's fluid balance, the œdema resolves and the intussusception reduces without further operative action. The diagnosis can be confirmed by giving the patient an ounce of barium to drink and 30–60 minutes later

procedure, and during the initial investigation of such cases the possibility of gastric or duodenal ulcer must usually be excluded.

It is often possible to demonstrate the varicosities projecting into the lumen of the œsophagus when a thin coating of barium has been left lining the œsophageal mucosa (see Fig. 161). It may be difficult to detect these small projections at screen examination and sometimes they will only be seen on films taken on expiration with the patient lying obliquely in the *recumbent position. Sometimes though* present they make no indentation in the œsophagus, in which case they lie in the peri-œsophageal veins rather than the submucosal veins. It is important to realize therefore that failure to detect or demonstrate œsophageal varices at barium examination does not exclude their presence.



Fig 161 Œsophageal varices

(2) Stomach and Duodenum

The value of radiological investigation in the discovery of lesions in the *stomach and duodenum is unquestioned.* The success of such investigations is dependent on careful and full screen examination by an experienced radiologist. Nevertheless, despite improvements in apparatus, advances in technique, and the most carefully conducted examination, it is possible still to miss small lesions. As a simple example, it is well known how barren are the results of barium examination of the upper alimentary tract following hæmatemesis.

In post-war years there has been a very considerable increase in the number of cases referred for barium meal examination and it is unfortunately all too true that with the increased out-patient work that has confronted clinicians and the welter of work referred for X-ray examination there has been a tendency for the clinician to give the radiologist less information, and for the radiologist to conduct his "lists of barium examinations" with insufficient clinical and laboratory knowledge of the case under investigation. Only if this trend is overcome can any real further advance be made. The ideal of consultation

should be requested when this lesion is suspected, and its presence will almost invariably be demonstrated by this route.

(3) The Small Bowel

Radiological examination of the small bowel is notoriously difficult and its results often unsatisfactory. Pathological conditions of the small bowel such as tuberculosis, regional ileitis, and tumours often become surgical emergencies before they are demonstrable. Meckel's diverticulum is rarely detected pre-operatively. Diverticulosis of the small bowel may be demonstrated though its extent may not be determined.

For satisfactory examination of the small intestine in the adult about two ounces of barium is the optimum amount of contrast medium, i.e. considerably less than is used in examination of the stomach. More than this tends to obscure rather than demonstrate small bowel lesions. Thus the technique for radiological examination of the small bowel differs from that for examination of the stomach and duodenum, and attempts to combine the two may lead to the missing of demonstrable pathology.

Examination of the small bowel, too, is a time consuming procedure requiring frequent films and screen examinations of the patient over a period of up to 5 hours or even more, and such examinations often require special arrangements to fit them into the time-table of a busy department.

It is important, therefore, that in making a request for a small bowel examination, a surgeon should have a clear conception of the pathological condition that he is considering, and the type of examination to which he is submitting the patient and which he is asking his radiological colleague to carry out.

(4) The Large Bowel

Radiologists have learned over the years that barium in bulk often obscures more than it demonstrates, and this applies especially to examinations of the colon. Techniques therefore have been directed towards obtaining mucosal pictures of the colon, and various practices such as the use of probanthine, tannic acid, veripaque, and air-replacement have been devised. Individual radiologists all have their own preference. All these procedures, however, are dependent on satisfactory preparation of the bowel in order to get rid of all fæcal material.

In spite of this it must be recognized that the detection of early lesions in the large bowel still leaves something to be desired. Large intra-luminal carcinoma, diverticulitis, established ulcerative colitis, intussusception, diffuse polyposis, and amœboma are conditions that are readily recognizable, should not be missed by radiological methods, and in the investigation of which this form of examination is a useful and essential diagnostic aid. But annular carcinoma, the early manifestation of intra-luminal carcinoma and single polypi are lesions that may not be detectable even at the most scrupulous and painstaking examination.

(*a*) **Ulcerative Colitis.** The early stages of this condition are often difficult to demonstrate radiologically as the mucosal œdema, swelling and hyperæmia can exist for a considerable time, producing marked symptoms, before any changes take place in the bowel wall which are detectable on the radiograph. Thus changes seen at

taking a radiograph of the stomach—an examination which can be carried out with a ward portable unit (see Fig. 163).

The chronic state is one which may not be suspected, and which may not be detected, for the intussusception if reducible may herniate into the stomach and be reduced several times during the course of an examination; in fact the radiologist may be able to produce and reduce the intussusception at will by palpation.

(*c*) **Anastomotic and Jejunal Ulcer.** An ulcer at the stoma or in the jejunum just distal to the stoma is often difficult to demonstrate, and the radiologist has usually to change his



Fig 163 Retrograde jejuno-gastric intussusception occurring seven days after gastro-jejunostomy had been performed

technique using considerably less barium than is usual in carrying out a barium meal examination. It is essential, therefore, when a request is made for a barium examination on a case that has previously had a gastrectomy, that the fullest details of the type of operation carried out should be given. The radiologist must be in full possession of all the available information when conducting his examination.

(*d*) **Gastro-colic or Gastro-jejuno-colic Fistula.** This rare late sequel to various forms of gastro-jejunal anastomosis is sometimes suspected clinically, and can be demonstrated radiologically. However, even if it exists, it is rare for the fistulous connection to be demonstrated by a barium meal examination. Barium enema is the examination that

haustrations or actual ulceration has taken place, that the *radiological confirmation* becomes possible. Thereafter, as the ulceration becomes more progressive, or pseudo-polypi become demonstrable and haustrations disappear from large segments of bowel, or as the muscle coat becomes involved and the bowel assumes a ribbon-like appearance, the radiological diagnosis is simple and conclusive. The rôle of radiological examination in the established case is:

(i) To demonstrate the length of bowel that is involved (see Fig. 164 (*a*)).



FIG 165. A polyp in the transverse colon well demonstrated by air insufflation following evacuation of the barium enema.

(ii) To show the stage that the disease has reached in all the segments of involved bowel, in particular where the disease has reached an advanced stage to show the ability of the bowel to contract and distend (see Fig. 164 (*b*)).

(iii) To show whether or not the terminal ileum is affected (see Fig. 164 (*b*)).

(iv) To detect malignant change should this arise, for carcinoma of the colon not uncommonly develops in long-standing cases of ulcerative colitis.

(*b*) **Polypi in the Colon.** Small adenomata may be flat and sessile or may become polypoid and pedunculated. They will commonly be obscured during complete filling of the colon with barium during a barium enema examination, and will only be detected on the mucosal films after evacuation of the barium or after air insufflation (see Fig. 165). As polypi not uncommonly undergo malignant change it is of considerable importance that they should not be missed. Unfortunately if preparation of the colon for the barium enema has not been effective a fæcal residue can produce an appearance indistinguishable



(*a*)



(*b*)

FIG 164. (*a*) Barium and air contrast in a case of ulcerative colitis affecting the transverse, descending and sigmoid colon and the rectum. There is no radiological evidence of involvement of the cæcum, ascending colon or proximal part of the transverse colon.
(*b*) Advanced ulcerative colitis affecting the whole colon There is also involvement of the terminal ileum.

from a polyp. It is in such cases that consultation between the surgeon and the radiologist is essential in the interests of the patient.

(*c*) **Hirschsprung's Disease.** This condition due to an aganglionic segment of sigmoid colon is now differentiated from megacolon, and its surgical treatment by recto-sigmoidectomy is an established practice. It sometimes presents in the first few days or weeks of life mimicking a neo-natal obstruction; but often the onset is insidious, with constipation and increasing abdominal distension becoming gradually more apparent. The differential diagnosis from megacolon is made by rectal examination, but once megacolon has been excluded it is essential to confirm the diagnosis of Hirschsprung's disease. This is done by barium enema examination, with in addition to the routine films, a radiographic demonstration in the lateral projection (see Fig. 166). This shows not only the narrow constriction at the recto-sigmoid junction or in the sigmoid colon, but also its length, which may in some cases be as much as 10 or 12 in.

In carrying out this examination it is important not to fill the colon completely with barium, as this may take several pints and will cause even greater colonic stasis. It is wise, also, to take a further film after evacuation, and if there is much barium residue to give colonic lavage until the residue is cleared.

DISEASE OF THE BILIARY TRACT

Radiological investigation of the biliary tract may be classified as pre-operative, operative, and post-operative.

(1) Pre-operative

(*a*) **The Technique of Cholecystography as a Diagnostic Test.** The test is well known and requires no full description; it consists of the oral administration of an organic iodine compound (there are many, Pheniodol, Telepaque, Priodax, Biliodyl, etc.), and the taking of films during a period ranging from 11–16 hours later. When a satisfactory demonstration of the gall bladder has been obtained, a further oral administration is given of a substance containing fat or oleum arachis, or even a meal with eggs and butter, and then subsequently further films are taken during and after contraction of the gall bladder. During the course of the examination films are taken with the patient both prone and erect.

If no satisfactory demonstration of the gall bladder has been obtained before administration of fat, and this failure of visualization is not due either to the patient having vomited the contrast medium or to pyloric stenosis a second dose of the compound can be given the following night and the whole procedure repeated. This will sometimes provide visualization of the gall bladder. Occasionally the oral contrast medium produces intestinal hurry or diarrhœa, but this rarely, if ever, interferes with absorption of the medium; poor concentration by the gall bladder should not be ascribed to this factor.

Tomography may be of very great help in obtaining good demonstrations of the gall bladder if it is being obscured by overlying fæcal and gaseous bowel shadows.

Cholecystography can only be regarded as a test of gall bladder function if the possibility of liver disease can be excluded. Further it is useless to carry out these investigations in the presence of jaundice as visualization of the gall bladder will not be obtained;

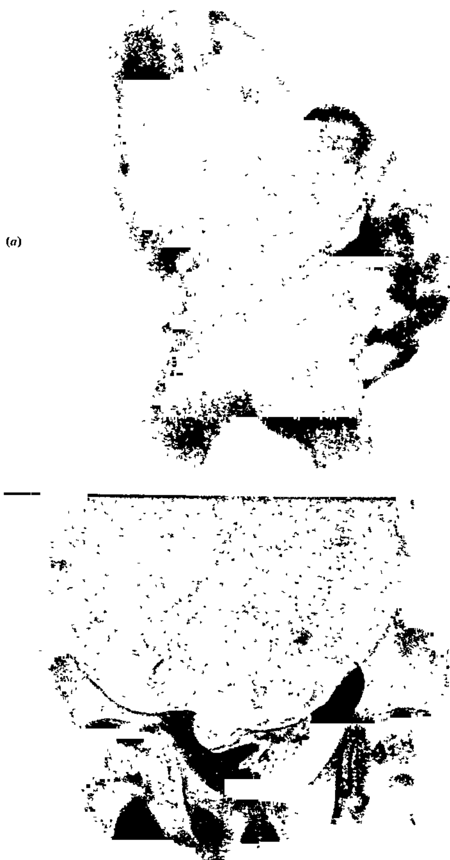


FIG 166 (*a*) Lateral projection during filling of the large bowel at barium enema examination showing the narrow segment at the rectosigmoid junction in a case of Hirschsprung's disease.

(*b*) A.P projection of the same case after evacuation of the barium showing the collapsed rectum and the grossly dilated sigmoid colon

from a polyp. It is in such cases that consultation between the surgeon and the radiologist is essential in the interests of the patient.

(c) **Hirschsprung's Disease.** This condition due to an aganglionic segment of sigmoid colon is now differentiated from megacolon, and its surgical treatment by recto-sigmoidectomy is an established practice. It sometimes presents in the first few days or weeks of life mimicking a neo-natal obstruction; but often the onset is insidious, with constipation and increasing abdominal distension becoming gradually more apparent. The differential diagnosis from megacolon is made by rectal examination, but once megacolon has been excluded it is essential to confirm the diagnosis of Hirschsprung's disease. This is done by barium enema examination, with in addition to the routine films, a radiographic demonstration in the lateral projection (see Fig. 166). This shows not only the narrow constriction at the recto-sigmoid junction or in the sigmoid colon, but also its length, which may in some cases be as much as 10 or 12 in.

In carrying out this examination it is important not to fill the colon completely with barium, as this may take several pints and will cause even greater colonic stasis. It is wise, also, to take a further film after evacuation, and if there is much barium residue to give colonic lavage until the residue is cleared.

DISEASE OF THE BILIARY TRACT

Radiological investigation of the biliary tract may be classified as pre-operative, operative, and post-operative.

(1) Pre-operative

(*a*) **The Technique of Cholecystography as a Diagnostic Test.** The test is well known and requires no full description; it consists of the oral administration of an organic iodine compound (there are many, Pheniodol, Telepaque, Priodax, Biliodyl, etc.), and the taking of films during a period ranging from 11–16 hours later. When a satisfactory demonstration of the gall bladder has been obtained, a further oral administration is given of a substance containing fat or oleum arachis, or even a meal with eggs and butter, and then subsequently further films are taken during and after contraction of the gall bladder. During the course of the examination films are taken with the patient both prone and erect.

If no satisfactory demonstration of the gall bladder has been obtained before administration of fat, and this failure of visualization is not due either to the patient having vomited the contrast medium or to pyloric stenosis a second dose of the compound can be given the following night and the whole procedure repeated. This will sometimes provide visualization of the gall bladder. Occasionally the oral contrast medium produces intestinal hurry or diarrhœa, but this rarely, if ever, interferes with absorption of the medium; poor concentration by the gall bladder should not be ascribed to this factor.

Tomography may be of very great help in obtaining good demonstrations of the gall bladder if it is being obscured by overlying fæcal and gaseous bowel shadows.

Cholecystography can only be regarded as a test of gall bladder function if the possibility of liver disease can be excluded. Further it is useless to carry out these investigations in the presence of jaundice as visualization of the gall bladder will not be obtained;

even with a history of jaundice having disappeared as long ago as 2 or 3 weeks, failure to visualize the gall bladder may still occur.

Interpretation of the results of cholecystography is not always simple, and should never be divorced from the clinical aspects of the case under investigation. The radiological investigation is not the final arbiter of gall bladder disease, but merely one factor in the full clinical examination of the patient. The following generalizations, therefore, though broadly true, must always be referred back to the patient under examination and interpreted in the light of all the clinical data, especially bearing in mind that pancreatic disease often interferes with gall bladder function and with demonstration of the biliary tree:

(i) The demonstration of gall stones is an indication of gall bladder disease. Non-opaque cholesterol stones, however, can occur in a gall bladder showing no signs of inflammation, but of course may give rise to biliary colic.

(ii) A well functioning gall bladder is an indication of normality and excludes the likelihood of chronic cholecystitis. Nevertheless just occasionally, probably in not more than 1 per cent of cases of chronic cholecystitis, the gall bladder will continue to concentrate the contrast medium well.

(iii) Non function by the gall bladder indicates gall bladder pathology and is usually evidence of chronic cholecystitis.

(iv) Impaired concentration by the gall bladder indicates gall bladder pathology, usually chronic cholecystitis. Grossly impaired concentration is not difficult to recognize, but lesser degrees of impairment may be difficult to decide. Most radiologists take an arbitary base line; a gall bladder shadow as dense as or denser than the shadow of the patient's lower ribs is regarded as evidence of normal function; a shadow less dense than the lower ribs is regarded as evidence of impaired function.

Failure of the gall bladder to contract after administration of fat should not be regarded too seriously as a criterion of impaired function. Individuals vary very considerably in their response. Failure to contract in the presence of poor concentration can, however, probably be regarded as further evidence in favour of pathology.

The main value of the films taken after administration of fat is that the altered gall bladder shape may bring to light gall stones not previously noted, and that the cystic and common ducts are frequently demonstrated.

(*b*) **The Technique of Combined Cholecystangiography.** This technique is coming into general use; it consists of oral cholecystography, as already discussed, followed by intravenous injection of 20 cc. of Biligrafin about 12 hours after the oral administration when the first film has already been taken, but before administration of fat. Further films are taken as required up to 40 minutes after the injection, to demonstrate the whole biliary tree. When this has been identified satisfactorily, fat is given, and the investigation proceeds as for oral cholecystography.

By this method the hepatic, cystic, and common ducts can be visualized as well as the gall bladder, and so a more comprehensive examination of the biliary tract carried out.

(2) Operative Examination of the Biliary Tract or Cholangiography

This procedure can be carried out, either in the operating theatre during cholecystectomy after insertion of a cannula, or some days later in the X-ray department when drainage has been carried out and a T-tube left in.

Injection of the contrast medium is made through the cannula or T-tube and thus a demonstration of the common duct and hepatic ducts obtained (see Fig. 167). The medium flows into the duodenum, and not uncommonly retrograde filling of the pancreatic duct occurs. The main use of this procedure is to demonstrate stones in the common duct.

There are two pitfalls in carrying out cholangiography. Air bubbles not uncommonly get into the cannula or tube and are carried along with the contrast medium into the



FIG. 167. Normal operative cholangiogram showing efflux into the duodenum as well as some reflux into the hepatic ducts. The normal tapering appearance of the distal end of the common duct at the sphincter of Oddi is well shown.

common duct. When a film is then exposed, these air bubbles are shown as *filling defects* in the contrast-filled common duct and may be misinterpreted as stones. This seems to occur more frequently with oily media than with watery media, and *for this reason* it is preferable to use diodone or any water soluble medium, rather than Neo-hydriol. Also it is wise to inject a reasonable quantity of the medium, say up to *12-15 cc.* in order to flush such air bubbles through into the duodenum *before making an exposure*. And finally, at least two films should be taken, *a further injection having been made between* the two exposures; air-bubbles *shift or change shape* with a further [illegible] remain constant.

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between 5–15 mm. A width greater than 15 mm. should be regarded as dilatation of the duct. The lower end of the common duct is poorly demonstrated in normal cases and appears funnel-shaped; this is the narrowest portion of the duct, being embedded in the head of the pancreas and the wall of the duodenum. A dilated duct usually loses its funnel shape and its lower end appears cigar-shaped, and is often well seen, in contrast to the poorly seen normal lower end. In normal cases the right and left hepatic ducts are usually not well seen, but are more readily demonstrated when some degree of obstructive dilatation of the lower biliary tree is present. An occasional cause of confusion is that the contrast medium, entering the duodenum and mixing with duodenal contents, sometimes passes retrogradely to the first part of the duodenum, pooling there, and casting a shadow that appears like a "re-forming" gall bladder.

The pathological changes that may be demonstrated in these cases are:

(*a*) Common duct stones which may be present in either an undilated or a dilated duct (see Fig. 168).

(*b*) Stones in the cystic duct remnant.

(*c*) Stenosis of the duct system. If strictures occur they are usually at the original site of entry of the cystic duct and are probably due to fibrosis following leakage of infected bile round the bile duct.

(*d*) Dilatation of the common duct without the presence of stones. Spasm of the sphincter of Oddi has been suggested as a cause in these cases, but it seems equally possible that the dilatation may have occurred before cholecystectomy and that any stones that were harbouring in the duct and causing obstruction have subsequently been passed.

URINARY TRACT

Radiological investigation of the urinary tract has now reached a high degree of accuracy, but this is dependent on a very strict observation of and control of technical factors.

The methods of examination include excretion urography, retrograde pyelography, and ureterography, renal arteriography, retro-peritoneal pneumography, renal puncture, and cysto-urethrography. So much useful information about the urinary tract, particularly the upper urinary tract, can be obtained by the routine use of these techniques and so much reliance has come to be placed upon them that it is absolutely essential that only first-class films from such investigations be considered acceptable. This can only be the case when there is the closest co-operation between surgeon and radiologist, and when the radiologist, who in most hospitals carries out the examination, is in full possession of the clinical facts of the problem under investigation.

The greatest aid in the everyday elucidation of clinical problems in this field is the use of excretion urography. Two important factors in the successful carrying out of this examination are the restriction of the patient's fluid intake prior to the examination, and the application of compression to the lower abdomen after the first post-injection film has been taken.

(1) Chronic Pyelonephritis

Recurrent urinary infection is sometimes the result of an unsuspected chronic pyelonephritis. Also hypertension may be the result of bilateral or unilateral renal disease, and in the latter case treatment by nephrectomy is sometimes successful. The

The other pit-fall arises from trying to do operative cholangiography in the theatre on bulky patients with portable X-ray apparatus of insufficient output. Films taken under such conditions are rarely of diagnostic quality and may be misleading. Cholangiography should only be carried out in the operating theatre if the conditions are ideal, or alternatively referred to the X-ray department if a drainage tube has been left in. If the investigation is to serve any useful purpose only films of the highest quality should be regarded as acceptable.

(3) Post-operative

The persistence or return of symptoms following cholecystectomy is one of the problematical clinical pictures with which surgeons are sometimes faced. The occurrence

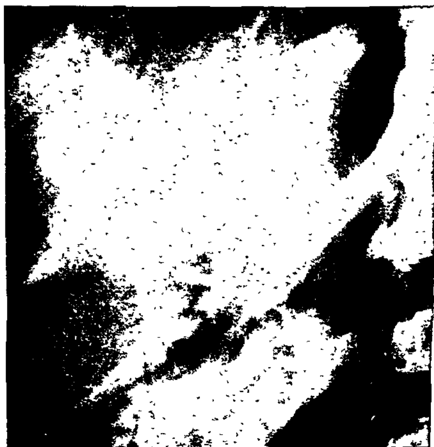


FIG. 168 Intravenous cholangiogram of a patient with symptoms of *dyspepsia and on whom cholecystectomy had been performed four years* earlier The common bile duct and common hepatic duct are dilated and contain multiple non-opaque gall stones

of persistent right hypochondriacal pain or of distension, or occasionally of jaundice, merit further investigation.

Intravenous cholangiography is the method of investigation in these cases. Either 40 cc. of Biligrafin or 20 cc. of Biligrafin Forte is injected and films taken at intervals during the hour following injection. By this method the common hepatic and common bile ducts can usually be visualized: the cystic duct stump may also be seen.

In normal cases the average width of the hepatic duct and of the common duct lies

(c) Diminished renal cortex. In good urographs the distance from the outer border of the kidney to an arc drawn through the tips of the minor calyces can be measured; this distance represents renal cortex and is usually equal in the two kidneys. In chronic pyelonephritis this distance may be diminished.

(d) Loss of the normal "cup" shape of the minor calyces, which become rounded and blunt.

(e) Elongation and narrowing of the minor and major calyces. This distortion of the normal calyceal pattern is quite characteristic of chronic pyelonephritis and is due to fibrosis with scarring within the renal substance.

(f) The presence of calculi. Often some small calculi are present in the minor calyces of the affected kidney.

All the changes described are not present in all cases of chronic pyelonephritis. Similarly, no single one of the appearances described is diagnostic of the condition, but the presence of two or more is highly suggestive of it.

(2) Renal Tumours

Some renal tumours reach considerable size before producing any symptoms or signs; others causing a brisk hæmaturia may subsequently be found to be no bigger than a walnut.

On the plain film the appearances which give rise to the suspicion of a renal tumour are deformity, enlargement or displacement of the renal outline, or occasionally speckled intra-renal calcification. On excretion urography the principal radiographic features are obliteration of calyces, elongation with either compression or dilatation of calyces, displacement of calyces, obliteration or dilatation of the renal pelvis, displacement of the pelvis and upper third of the ureter, or non-filling of the calyces and pelvis.

The differential diagnosis of a space occupying lesion in the kidney is often not possible from excretion urographs, and any attempt on the part of the radiologist to give emphasis either to a diagnosis of solitary cyst or renal carcinoma may be misleading and not in the best interests of the patient. Nevertheless, cases arise when the surgeon would prefer not to embark on an exploratory operation if the space-occupying lesion is a solitary cyst; for example, in the routine pre-operative examination of a case of prostatism excretion urography may bring to light a silent renal "tumour"; the surgeon may be unwilling to submit an elderly patient to further surgery if the diagnosis is not established as being renal carcinoma.

Renal arteriography with serial films of the kidney taken during the arterial, capillary and venous phases will usually establish the diagnosis. To carry out this procedure special apparatus is required to take serial films rapidly. Injection of diodone is made rapidly either direct into the aorta by the translumbar approach, or into the renal artery after insertion of a Seldinger catheter into the femoral artery which is then threaded in a retrograde direction until it reaches the level of the renal vessels. By this method, tumours such as adeno-carcinoma show a mottled "pooling" of the contrast medium within the substance of the space-occupying lesion, which persists into the capillary and venous phases. A space-occupying lesion which however is due to a renal cyst, is avascular, and shows as a defect in the capillary or nephrogram phase. A simpler technique, requiring no special apparatus for differentiating between growth and renal cyst in such cases is the procedure of renal puncture which can be carried out as follows:

investigation of hypertension in the younger age groups, nowadays, invariably includes investigation of the urinary tract by excretion urography. The radiological appearances of chronic pyelonephritis therefore are of some importance and are not sufficiently well recognized (see Fig. 169).

They are as follows:

(*a*) Asymmetrical concentration by the kidneys on the film taken 5 minutes after

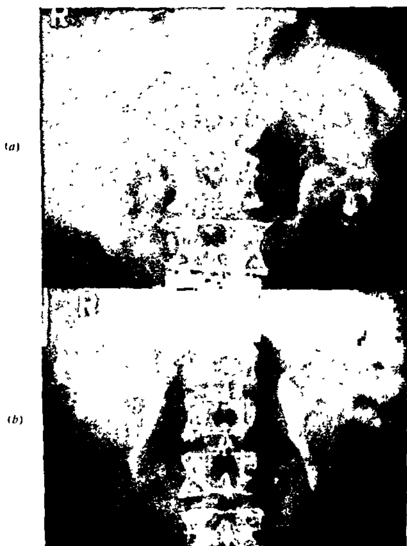


FIG 169 (*a*) Bilateral chronic pyelonephritis demonstrated by excretion urography.
(*b*) Excretion urogram showing chronic pyelonephritis of the right kidney which is contracted, has dilatation of its minor calyces and distortion and narrowing of its major calyces

intravenous injection of the contrast medium; the pathological kidney may show slightly impaired concentration at this stage. This film should be taken *before* compression is applied to the abdomen.

(*b*) The demonstration of a contracted kidney. In most individuals the two kidneys are practically identical in size. In chronic pyelonephritis the affected kidney is often contracted.

(v) Two or 3 cc. of contrast medium are then injected into the lesion. In the case of a cyst the cavity is outlined, and its size can be compared with the original urograph. In the case of a neoplasm, the contrast medium is shown to track irregularly within the tissue (see Fig. 170).

This technique obviously has a limited application, and it is likely that in many cases, surgeons will prefer to undertake exploration. Nevertheless, occasions will arise when the procedure can usefully be employed, and it has come to take its place in the full array of radiological investigations.

(3) Urinary Calculi

Urinary calculi usually contain calcium in some form and so cast a shadow on a radiograph. Their site and effect on renal function can be determined by excretion urography. By this method, therefore, it can be shown whether they are single or multiple,



FIG 171 Excretion urography eight days after an attack of right sided ureteric colic. The left kidney is normal The right kidney shows as a nephrogram or "white kidney." There was a small calculus at the lower end of the right ureter which was subsequently passed. A follow-up pyelogram showed that the right kidney had returned to normal

unilateral or bilateral, calyceal, pelvic, ureteric, or vesical. It can also be shown whether there is a chronic pyelonephritis or hydronephrosis associated with the calculus, whether there is impairment or loss of renal function. The whole urinary tract can thus be assessed and the course of treatment to be adopted can be decided. After either their removal by surgical methods or their passage by the normal route, the improvement of renal function and form can be observed and recorded, and by subsequent follow-up it can be seen whether or not a calculus is re-forming.

Similarly the passage of a calculus down the ureter can be observed, and the development of any obstructive changes noted.

(i) An intravenous injection of 20 cc. of diodone or hypaque is made in order to produce a pyelogram.

(ii) A metal marker graduated in centimetres is put on the patient's skin, and lateral

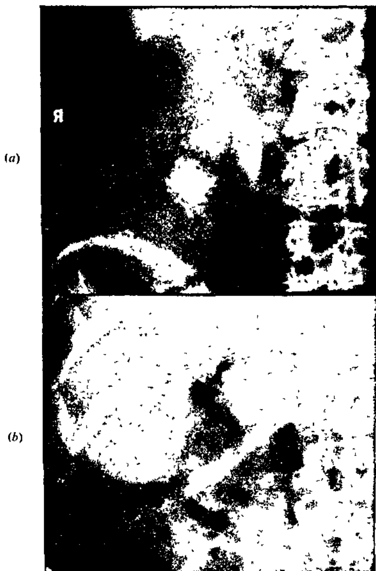


FIG 170 (*a*) Renal puncture in a case of carcinoma of the kidney showing the injected contrast medium tracking irregularly in the tumour Excreted contrast medium from the preliminary intravenous injection can be seen in the renal pelvis

(*b*) Renal puncture in a case of renal cyst, showing the smooth round shape of the cyst wall

and postero-anterior films are taken. From these the exact site and depth of the kidney and its space-occupying lesion can be estimated accurately.

(iii) A needle is introduced from the back so as to enter the kidney in the region of the suspected lesion and is aimed under screen control towards the "tumour."

(iv) If the needle enters a cyst, straw-coloured fluid is aspirated whereas in the case of a neoplasm blood is aspirated.

(v) Two or 3 cc. of contrast medium are then injected into the lesion. In the case of a cyst the cavity is outlined, and its size can be compared with the original urograph. In the case of a neoplasm, the contrast medium is shown to track irregularly within the tissue (see Fig. 170).

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Similarly the passage of a calculus down the ureter can be observed, and the development of any obstructive changes noted.

The calculi most easily missed are ureteric calculi, especially small calculi in the lower part or intra-mural part of the ureter. A useful radiological sign when it occurs, is the appearance of a nephrogram on the affected side, the so-called "white kidney," while the other side remains functioning normally (see Fig. 171). This implies acute ureteric obstruction, usually due to impaction of a calculus in the ureter, and is caused by the damming back of the contrast medium in the renal capillaries. When therefore a unilateral nephrogram is seen during excretion urography search must be made for the ureteric calculus until it is discovered.

Often acute renal colic may be caused by minute calculi or crystals, or by the passage of small clots—none of which will be demonstrated on the radiograph. Furthermore, severe renal colic often impairs renal function considerably or even suppresses it. Excretion urography therefore serves little purpose in the period immediately after an attack. In doubtful cases, plain X-ray examination of the urinary tract may sometimes be helpful in demonstrating a ureteric calculus and thus confirming the cause of the colic as being in the urinary tract. But it is wiser to delay excretion urography until 5–7 days after the attack; if it is carried out immediately after the attack no information is likely to be obtained that will influence the course of treatment, and if no demonstration is obtained of the function of the kidney on the affected side it will be necessary to repeat the examination later. Whereas if the examination is delayed for a few days it is probable that the calculus or whatever is causing the colic will have been passed and renal function will have had time to recover, thus rendering possible a true record of the state of affairs.

(4) Prostatic Hypertrophy

In all patients complaining of symptoms due to an enlarged prostate, with the exception of those in whom a severe degree of renal failure makes the examination useless, excretion urography forms part of the routine investigation in assessing them. In assessing such patients clinical examination reveals only the gross abnormality whereas it is necessary to be able to detect early and less obvious changes. The information which can be provided by this radiological method is a refinement of the ordinary methods of clinical examination of the urinary tract, and may be considered as follows:

(*a*) **Renal Anatomy.** Before dealing surgically with the lower urinary tract, the surgeon requires to know that he is dealing with a normal upper urinary tract. He wants to know that both kidneys are present, that they are not hydronephrotic, and that they do not harbour an alternative cause for hæmaturia, such as a stone or growth, in a man with prostatic enlargement

(*b*) **Renal Function.** It is important to know that both kidneys are excreting and concentrating well. Although laboratory tests may show the blood urea level to be raised, they give no indication of its cause which may be due to chronic pyelonephritis or to hydronephrosis from back-pressure. If the blood urea level is above 120 mg. per cent it is unlikely that concentration of diodone will occur, but up to that level often useful information regarding the kidneys can be obtained. It is useful to know whether a hydronephrosis exists, which may be expected to improve after adequate drainage, or a pyelonephritis, indicating renal failure without obstructive dilatation, which will not recover under any circumstances. Excretion urography, too, gives a good visual record of improvement following drainage.

(c) **Ureteric Function.** Stasis in the lower end of the ureters or persistent filling of the whole length of both ureters in the presence of good excretion usually occurs with a significant amount of residual urine in the bladder, and is a warning that the beginnings of renal failure are imminent.

(d) **Bladder Anatomy.** A thick-walled bladder results from long-continued obstruction and occurs often with gross trabeculation and saccule formation (see Fig. 172). Its



Fig. 172. Cystogram 30 minutes after injection in excretion urography showing hypertrophy of the wall as a ring shadow outside the filled cavity of the bladder.

demonstration eliminates the possibility of an atonic or paralytic bladder, and warns of the possibility of infective complications following operation, due to stagnant blood and urine in deep saccules.

Similarly, growth, diverticulum, or stone in the bladder, the classical complications of an enlarged prostate, may be demonstrated radiologically and often require treatment as a staged procedure before the prostate. It is true that all these things are visible with the cystoscope, but it is not desirable to perform cystoscopy in the presence of a very enlarged prostate before the actual time of operation for fear of inducing acute retention, and it is not possible to assess the size of a diverticulum with the cystoscope. The bladder demonstration during excretion urography will almost always demonstrate stone or diverticulum, and will often demonstrate the presence of a large growth.

(e) **Bladder Function.** The presence of residual urine after micturition can be demonstrated by this method, and a fair assessment of its amount can be made. This eliminates the need for instrumentation.

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FIG 173 Cystogram 30 minutes after injection in excretion urography showing a sacculated bladder and a large intra-vesical projection of the middle lobe of the prostate



FIG. 174. Osteoblastic metastases from carcinoma of the prostate affecting the of the pelvis

(*f*) **Prostate Anatomy.** Rectal examination reveals lateral lobe enlargement; if middle lobe enlargement exists, the information derived from rectal examination can be supplemented by the demonstration of its mid-line intravesical projection as a filling defect in the cystogram (see Fig. 173). Similarly, the presence of prostatic calculi can be shown, and the knowledge of their presence may be of help in deciding whether or not a hard area in the prostate is malignant or not.

Finally, in carcinoma of the prostate, the demonstration of osteoblastic skeletal metastases may establish the diagnosis when the serum acid phosphatase estimation is unhelpful, and the course of such metastases can be observed graphically under treatment (see Fig. 174).

BONE

With the great specialization that has taken place within the broad realms of surgery most bone and joint diseases have tended to become the prerogative of the orthopædic surgeon. Nevertheless in routine practice in general surgery, the practising surgeon is faced with many problems in which bone pathology is an important element. The radiological aspects of several of these are discussed here.

(1) Inflammatory Conditions

(*a*) **Osteomyelitis.** Acute osteomyelitis is usually diagnosed and treated before radiological signs develop, as it takes at least 7 days and sometimes more before bone changes appear. Antibiotic-therapy is now so effective that it is not uncommon for a case of acute osteomyelitis to be admitted to hospital, treated and discharged without there being any radiological evidence whatsoever of bone disease.

Sometimes, however, bizarre and uncommon pictures present when antibiotic therapy has been inadequate. Occasionally, such cases present many weeks or months later, with a constant limb pain, but no very definite localizing signs; this type of case is usually one that has not reached hospital in the first instance and whose acute infection was dealt with by domiciliary treatment.

Often the radiological appearance in such cases is merely of a cortical thickening along part of the shaft of the affected bone. This cortical thickening may be only slight or markedly proliferative, and it may even have layered new periosteal bone on its surface. Because of the clinical presentation, the clinical signs, and the unusual radiological appearance, the differential diagnosis is difficult; the possibility of malignant conditions such as reticulo-sarcoma, Ewing's tumour and metastatic neuroblastoma must be considered, and obviously early diagnosis is important for treatment differs. There are no radiological signs which, *per se*, divorced from the history and clinical course, are diagnostic. As a generalization, it can be said that in local osteoperiostitis of the type being discussed, the cortical thickening is usually dense, medullary changes are rare, layered periosteal new bone is rare, and the condition is usually not progressive. If there is destruction of medullary bone with formation of new periosteal bone, and the condition is shown over a short period of observation to be progressive, all in the absence of clinical signs consistent with an acute inflammatory process, then the diagnosis lies elsewhere and it would be wise to undertake bone biopsy.

(*b*) **Osteitis of a Phalanx.** In the presence of an acute or chronic paronychia or cellulitis of a finger the question may arise whether or not there is bone infection or necrosis.

When the bone is infected it becomes intensely hyperæmic; hyperæmia of bone always produces an osteoporosis. So the affected phalanx becomes extremely osteoporotic; the bony trabeculæ in it may be absorbed and be no longer visible, the bone remaining apparently merely as a faint shell of cortex. Osteoporosis of such a degree is not an indication of bone necrosis but merely of inflammation. If treatment is successful a phalanx involved even to this extent can undergo repair and complete bony re-constitution can take place. The only radiological indication of necrosis of part of a phalanx is when that part separates, and by contrast appears denser than the parent fragment; this is an indication that it is avascular and has been sequestrated.

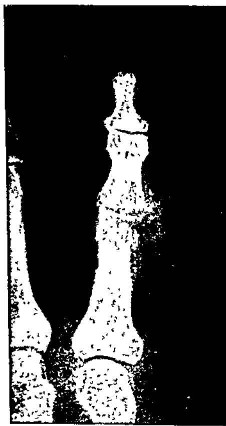


FIG 175 Osteitis affecting the proximal and middle phalanges of the fifth digit with inflammatory destruction of the intervening joint

The other valuable feature of X-ray examination of digital osteitis is the demonstration of whether or not the adjacent interphalangeal joint is involved. When the joint becomes affected articular cartilage is destroyed and the joint space becomes narrower than the corresponding joint of the next finger (see Fig. 175). In addition, sometimes a break or defect can actually be seen in the sub-articular bony cortex. Knowledge of the state of the joint allows the surgeon to prognose and may influence his course of treatment.

(*c*) **Bone Changes in Diabetes.** The bone and joint changes that occur in diabetes, notably in the feet, had long been regarded as Charcot's joints due to diabetic neuropathy. It is now known, however, that these changes are predominantly inflammatory and not neuropathic. This is of considerable importance, for, of course, the inflammatory process can be arrested at any stage by controlled antibiotic and anti-diabetic treatment thereby allowing surgical toilet of the condition, and the retention of what appears to be a hopelessly damaged foot.

The process is as follows. An acute or low-grade infection begins near the bone, often near the weight bearing metatarso-phalangeal joints. The port of entry may be a perforating ulcer, a septic corn, or diabetic cutaneous gangrene. Superficial lesions may heal well, but deep sepsis can still persist tracking along the periosteum. Radiologically a local osteoporosis develops. Soon a break occurs in the cortex and an osteitis ensues. At this stage there is often a periosteal reaction along the involved metatarsal; (see Fig. 176 (*a*)), this proceeds to progressive destruction of the head of the bone, then of the medulla of the adjacent shaft. The cortical walls approximate producing a tapering appearance (see Fig 176 (*b*)). The process may be arrested at any stage, or may progress to very gross destruction. Repeated weight bearing on the denervated foot does not help repair nor does the poor blood supply which is a frequent accompaniment.

(*d*) **Osteitis Pubis.** Occasionally after either retro-pubic or supra-pubic prostatectomy this painful condition arises. The symptoms may start anything from 2 weeks to 3 months



(a) (b)

FIG 176 (a) Inflammatory changes producing osteoporosis, bony destruction and a periosteal reaction around the 3rd metatarso-phalangeal joint in a diabetic with an ulcer on the sole of the foot

(b) Tapering of the proximal phalanx and destruction of the inter-phalangeal joint of the great toe in a diabetic with a history of repeated cellulitis of the foot. There was no clinical evidence of neuropathy



(a) (b)

FIG. 177. (a) Osteitis pubis affecting both sides of the symphysis Film taken four months after retro-pubic prostatectomy

(b) Osteitis pubis causing at this stage only loss of cortex along the left side of the symphysis. 10 weeks after retropubic prostatectomy

after operation. It may cause pain in the perineum or over the ischial tuberosities, pain referred down the thighs or even down the legs, or pain on micturition or defæcation. Signs are usually few or absent, though in some cases there is pain on pressure over the symphysis pubis.

Radiologically it manifests itself as a loss of cortex on one or both sides of the symphysis pubis followed by an osteoporosis of sub-cortical bone (see Fig. 177). This is followed by a sclerotic reaction in sub-cortical bone and dense re-ossification of the area of affected bone, sometimes leading to complete bony fusion across the symphysis.

The clinical condition rarely responds to specific therapy, and it may take twelve months to settle. The radiological course of the condition usually takes 12–18 months before final bony consolidation is established.

(2) Malignant Bone Diseases

Primary malignant disease of bone in the form of osteogenic sarcoma and chondrosarcoma requires no mention here, but reticulo-sarcoma is worthy of discussion.

(*a*) **Reticulo-sarcoma.** This condition may occur as (i) a single primary focus in bone, (ii) multiple primary foci in bone, or (iii) primary soft tissue reticulo-sarcoma secondarily involving bone. The tumour is radio-sensitive and the results of treatment of group (i) are eminently satisfactory, of the other two groups less satisfactory, though still a practical procedure.

Differential diagnosis may be a difficult problem, for the clinical presentation is often indefinite and the radiological picture unequivocal. The differential diagnosis is usually from an inflammatory process. In reticulo-sarcoma the cortical and periosteal changes are secondary to medullary changes. The condition commences in the medulla as a localized group of small translucencies, with ill-defined margins; these extend along the shaft and become confluent locally. Small areas of increased density may be scattered irregularly within the affected bone. The cortex is then involved by contiguity in a patchy way later becoming progressively destroyed (see Fig. 178). Periosteal new bone may appear, with possibly a small reactive triangle of periosteal new bone at the edge of the lesion, but as a rule periosteal new bone is not extensive in this condition.

(*b*) **Metastatic Carcinoma in Bone.** The demonstration and observation of metastatic carcinoma in bone is not now such an academic pursuit as once it was, for the treatment of multiple metastases from breast, prostate, and thyroid, and solitary metastases from kidney have all met with a measure of success.

Metastases from carcinoma of breast are usually osteolytic and are commonly widespread. Any bone may be involved, but the vertebræ and the ribs are frequently the site of metastases. The secondary growth usually starts in the medulla, destroying bony trabeculæ, producing a translucent zone in the bone; it increases in size, destroying cortex by direct spread. Pathological fractures through such secondary growths, and especially producing compression deformities of the vertebral bodies, are common. The condition is progressive, whole bones being destroyed by the coalescing of adjacent metastases.

Arrest of the progress of the destructive process is often observed radiologically following adrenalectomy, and in some cases consolidation of bony tissue with the laying down of dense abnormal bony trabeculæ occurs The gross effect and course following surgery can therefore be assessed alongside clinical improvement.

Similarly following radiotherapy or testosterone therapy, the arrest and recalcification of osteolytic lesions may be observed, and after testosterone therapy dense sclerotic new bone is sometimes laid down in the whole soft tissue mass that was originally metastatic new growth, often extending beyond the original confines of bony skeleton.



FIG. 178 Single primary reticulo-sarcoma of the upper end of the humerus.

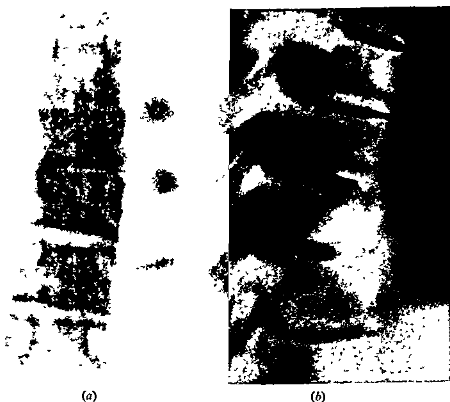
Occasionally metastases from breast carcinoma are osteoblastic at the onset. These may be equally widely disseminated but are rarely the cause of pathological fracture.

Metastases from carcinoma of the prostate are usually osteoblastic. When a clinical diagnosis of carcinoma of the prostate has been made on rectal examination, but the serum acid phosphatase remains low, confirmatory evidence may be obtained by the demonstration of osteoblastic metastases in the pelvis or spine. The arrest of the progress of such metastases under stilbœstrol may be assessed radiologically; occasionally they have been observed to disappear entirely. The differential diagnosis between these metastases and Paget's disease may be difficult, but if acid and alkaline phosphatase estimations are unhelpful, the opinion of an experienced radiologist will usually prove to be right.

Metastases in bone from thyroid may present clinically as solitary lesions, shown radiologically to be osteolytic (see Fig. 156). Similarly metastases from carcinoma of the kidney sometimes present as a solitary osteolytic lesion in a long bone and some success has been reported by amputation of the affected limb and nephrectomy. In this latter condition the primary growth may be silent, and the case present as a pathological fracture. Such metastases are commonly large osteolytic lesions, with well defined edges, arising in the medulla, eventually breaking the cortex.

(3) The Spine

Radiological interpretation of diseases of the spine is not always a simple matter, especially when the disease process, though sufficiently advanced to produce symptoms



(*a*) (*b*)

FIG 179. Tomographs of the mid-thoracic spine in a case of tuberculosis showing caries in adjacent vertebral bodies, destruction of the intervening disc and a wide paravertebral shadow.

and signs, is still in a relatively early stage, and bone and joint changes are minimal. In the thoracic spine the overlying shadows or ribs and lungs may cause confusion, in the cervical region the super-imposition of the shadows of the transverse processes and articular facets cause difficulty, and in the lumbar spine the projection of bowel shadows over the vertebræ render interpretation difficult. Routine radiographic procedures will usually overcome these difficulties but if doubt still lingers regarding the state of the spine after thorough scanning of the conventional films, or if for permanent record it is required to have an accurate demonstration of the state of a pathological process, tomography of the spine will provide the answer. This is a precision technique and is time consuming, but a minute "dissection" of the spine can be carried out by this method.

For example, if a child in the 10–15 years age group is complaining of an ache in the back, and clinical examination reveals a kyphosis, limitation of movement and tenderness over the lower thoracic spine, the possibility of tuberculosis of the spine arises. X-ray examination of the spine may reveal deformity of the lower thoracic vertebral bodies with narrowing of the intervertebral spaces. However, juvenile osteochondritis (or epiphysitis) of the spine can produce a similar clinical and radiological picture. The treatment



(a) (b)

FIG. 180 Tomographs of the mid-thoracic spine in a case of juvenile osteochondritis showing herniation of the nucleus pulposus into a vertebral body, narrowing of the relevant disc, but no increase in the width of the para-vertebral shadow

and prognosis differ widely, and accurate diagnosis is essential. Tomography of the spine will reveal the true nature of the condition. Tuberculosis is a destructive process, often involving the opposing surfaces of adjacent vertebral bodies, producing in the early stages no bony reaction or sclerosis; the edge of the destructive lesion in bone is ill defined; the intervening disc space narrows due to destruction of its substance, and early there develops a para-vetrebral abscess producing widening of the para-vertebral shadow in the thoracic region or a psoas bulge in the lumbar region (see Fig. 179). Osteochondritis is due to interference with the blood supply to the cartilaginous end plate which necroses, breaks, and allows the nucleus pulposus to herniate through the break into the spongiosa of the vertebral body; there is an immediate bone reaction producing a sclerotic ring of bone sealing off the herniation. Interference with growth of the vertebral body occurs, with increased growth in an antero-posterior direction, a temporary cessation of vertical growth producing a wedge-shaped vertebra There is never any increase in the para-vertebral shadow or psoas bulge in this condition (see Fig. 180).

Similarly tomography will help to elucidate other conditions of the spine, such as anomalies and injuries in the atlanto-axial region, injuries to any region of the spine, primary tumours such as osteoclastoma, or metastatic spread, diastomatomyelia, neurofibromata, etc.

Against this, routine conventional radiography is usually eminently satisfactory for the demonstration of such conditions as hæmangioma (the large venous plexus of which



FIG. 181. Radiograph of the lumbar spine showing a defect in the pars inter-articulatis of a vertebra—spondylolysis.

may be the cause of severe symptoms and signs), spondylolysis (see Fig. 181) spondylolisthesis, osteo-arthritis of the diarthrodial joints, spondylosis, and the exclusion of other pathology in cases of suspected posterior disc herniation.

FEMORAL ARTERIOGRAPHY

Although the risks of peripheral arteriography are small, the indications for its use are few. Much information can be obtained by clinical examination and oscillometry, and arteriography should only be undertaken when further and more exact information is required which will be of benefit to the patient.

The technique is as follows:

(a) Femoral arteriography is carried out under spinal anæsthesia as this prevents spasm which may otherwise be induced by an injection of diodone.

(b) The injection is made percutaneously. A Harris's lumbar puncture needle with a stilet projecting a few millimetres beyond the point of the needle is used. The femoral

artery is entered with the point of the needle directed proximally, and as soon as it is clear that the needle is in the lumen, the stilet is introduced and the needle is threaded up the artery for at least a centimetre. It is thus firmly within the arterial lumen and need not be held in place. By introducing the needle in a proximal direction there is no possibility



FIG 182 Femoral arteriogram showing an arterial graft following a tear of the artery due to the fracture of the femur in a 14 year old boy with severe multiple injuries The graft subsequently thrombosed

that it may be directed into the profunda femoris with consequent lack of filling of the main femoral artery.

(*c*) The syringe is then connected to the needle by a length of pressure tubing to enable the injector to stand out of the range of the X-radiation, and 20 cc. of 50 per cent diodone injected as quickly as possible, preferably within 4 seconds.

(*d*) By means of a cassette tunnel serial films are then taken along the length of the limb, thus demonstrating in turn the femoral artery, the popliteal artery, the tibial arteries, and the arteries of the foot.

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(*d*) Changes in the rate of flow.

(*e*) Occlusion of an artery. This is usually the result of thrombosis secondary to atheroma. The thrombosis, which appears clear-cut on the arteriogram, usually spreads proximally to the origin of a branch artery through which the flow is deviated. The collateral circulation, often dilated and tortuous, is usually shown.

(*f*) The state of the circulation after arterial graft (see Fig. 182).

(*g*) Arterial aneurysm. Care must be taken in the interpretation of the appearances obtained, for the aneurysmal sac may be filled with laminated thrombus and the radiographic demonstration may show no more than a shallow bud from the lumen of the artery.

(*h*) Arterio-venous fistula. This condition presents one of the most characteristic pictures in clinical surgery, and arteriography is not required for its diagnosis. It may be a useful procedure, however, to locate the precise anatomical position of the lesion as an aid to the surgical approach (see Fig. 183).

Arterial embolus is a condition with a clear and dramatic history and characteristic physical signs. Angiography (either aortography or arteriography) is not required in making a correct diagnosis. The operation of embolectomy should be performed as soon as possible after the circulation is interrupted and radiological investigation will only impose delay. Further, though arterial injection is comparatively safe under most circumstances, it may cause thrombosis in the stagnant column of blood which exists proximal to a recent block. In this condition, therefore, angiography is considered to be contra-indicated.

PROTECTION

The increased use of X-radiation for diagnostic purposes has made protection against X-radiation an important consideration. Radiologists and radiographers are trained to practise routine protection methods in their normal daily work, and the greater danger probably arises in relation to casual users and to patients. The danger to casual users lies mainly in receiving direct radiation, which over the years is cumulative, and may produce radiation effects.

Surgeons may fall into the category of casual users, especially if they are in the habit of carrying out such procedures as arteriography, Smith Petersen pin operations, operative cholangiography, or other operative procedures requiring X-ray control.

The code of practice to adopt should be:

(*a*) Never allow any part of the body, and especially the hands to be in the direct X-ray beam during an exposure.

(*b*) Avoid scatter radiation as far as possible, preferably by standing at least 6 feet away from the direct X-ray beam during an exposure.

(*c*) If in the habit of conducting many examinations where some exposure cannot be avoided, for example operative cholangiography, ask the radiologist to test the dose of radiation being received.

The danger to patients is mainly the cumulative effect on the gonads, which may produce genetic effects not apparent immediately but which only produce their biological results in the second and third generations.

The dose to the gonads arises in such examinations as X-ray of the lumbar spine (in females), pelvis, hip, excretion urography, barium enema, etc. A recent M.R.C.

Pressure is not applied to the artery at any time during the injection as compression of a diseased artery together with the injection of diodone may accentuate the liability to thrombosis. Light digital pressure for 2 or 3 minutes after withdrawing the needle prevents the formation of a perivascular hæmatoma.

By this method it is possible to demonstrate:

(*a*) Anatomical variations of the vascular tree.

(*b*) Irregularity of contour of the vessels, consisting of small protrusions into the lumen;



FIG 183. Femoral arteriogram showing an arterio-venous aneurysm in the popliteal fossa. There is very marked hypertrophy and dilatation of the femoral and popliteal arteries and the site of the arterio-venous anastomosis is well shown.

these represent intimal thickening due to atheroma with or without super-imposed thrombus, and are especially common at the origin of a branch where it may cause a characteristic constriction or "nipping."

(*c*) Variations in calibre. The calibre of the artery may be increased or decreased although the contour retains its normal smooth outline. An increased calibre indicates hypertrophy of the vessel such as occurs in collateral branches if the main artery is occluded, or in arteries proximal to an arterio-venous fistula. Vessels of an abnormally fine calibre may be seen in thrombo-angiitis obliterans.

CHAPTER IX

RADIOTHERAPY IN THE TREATMENT OF MALIGNANT DISEASE

G. W. Boden

CHOICE OF RADIAL TREATMENT METHOD

The patient suffering from malignant disease can only be cured by surgical excision of the growth or by destruction of it by radiation. The choice of which of these methods is to be employed must therefore be considered most carefully for every patient and the relative probability of cure by the two agents must be assessed as accurately as possible. Experience has shown us that comparatively rarely can subsequent radiotherapy rectify ill-judged surgery, and similarly, ineffective irradiation can only be put right by later surgery in certain cases. As is well known, second attempts at excision of neoplastic disease, after the initial excision has resulted in recurrence, are seldom followed by complete cure, and this also is true of radiation. Second curative radiation attempts indeed are usually not possible. The object therefore is to select the method, either surgical, radiotherapeutic, or combined which will extirpate the malignant growth at the *first* attempt, or which will provide the greatest chance of achieving this.

It must initially be decided whether treatment of any active kind is called for, and while this may be clear from the surgical viewpoint, it is not sufficiently appreciated that many patients with advanced malignant disease are also best left untreated by radiation. This is particularly true in advanced disease unaccompanied by major symptoms, and in those varieties of neoplasm which are known to be comparatively unresponsive to radiation.

If some radiotherapeutic response may be expected, the incurable case can be treated palliatively by radiation, weighing up carefully the benefits and the extension of life obtainable against major symptoms that the radiation may cause. In many varieties of malignant disease, years of useful and symptomless survival can be obtained by judicious radiotherapy, although it is known from the beginning that cure is impossible. The uses of surgery in the palliation of advanced cancer must also not be forgotten, and the partial removal of growths which are causing pressure symptoms, or are fungating, is often helpful to the patient, especially if used with subsequent irradiation.

In making the choice between surgery, radiotherapy, or combined surgery and radiotherapy in the curative treatment of malignant disease, there are three principal factors to be taken into account—

(1) Tissue of origin and site of neoplasm.

(2) Degree of advancement.

(3) Histological character.

These three factors are not independent, and must be considered in relation to one another.

Committee has recommended that the total life dose received by any one individual should not exceed 200 r (Rontgens), and that before the age of 30 years, that is to say while the major part of the individual's likely procreation lies in the future, the total dose should not exceed 50 r.

With this in mind it is worth remembering that the dosage administered to the gonads in many of the routine examinations, while obviously it must vary from department to department, is probably of the order:

Lumbar Spine	700 mr. (milli-röntgens)
Pelvis	1000 mr. (milli-röntgens)
Urography	1200 mr. (milli-röntgens)
Barium Enema	500 mr. (milli-röntgens)

(3) Histological Character

Sensitivity to radiation, in general, decreases as degree of differentiation in the cells of neoplasms increases. This radiotherapeutic maxim is undoubtedly a better guide to the use of surgery rather than it is an indication of how curative radiotherapy will be. Anaplastic tumours should not be dealt with surgically in the first instance, as recurrence is almost inevitable, though their radiosensitivity does not necessarily indicate a high radiocurability. On the other hand well-differentiated neoplasms are less likely to recur locally if adequately excised.

Of the carcinomas, adenocarcinoma is usually radio-resistant, and surgical treatment frequently preferable. Squamous carcinoma is of moderately high resistance, but provides many radiation cures when the site is an accessible one. Most other carcinomas range from moderately sensitive to very sensitive, depending on the degree of differentiation, and embryonal growths are very responsive to radiation.

Of the sarcomas, those arising from lymphoreticular tissue are of moderate to high radiosensitivity, and because of their rapid growth and liability to widespread metastases, are far more suited to radiotherapy than to surgery. The sarcomas of the supporting tissues are uniformly radio-resistant and surgery is the treatment of choice. Teratomas are a field for surgery and are basically radio-resistant though radiation may have some effect in restraining growth, depending upon the particular tissue which is actively malignant.

It must be realized that exceptions to what has been said will not be uncommon. Each patient must be considered individually, and the case assessed when the full extent of the disease has been determined and the histology studied. Neoplasia in children is usually radiosensitive whatever the histological character of the disease.

It must also be borne in mind that a course of radiation therapy, especially if directed to the trunk and for a deep-seated neoplasm is likely to be debilitating to an already ill patient. Radiation sickness may be caused, though this is far less of a problem than formerly, while anæmia and loss of weight and strength must be anticipated to a degree depending upon the nature and extent of the neoplasm. Unavoidable damage to normal structures by radiation may take place which may give rise to symptoms. Surgery does not necessarily have comparable disadvantageous effects on the patient, and as a consequence may be the preferable method of approach in certain cases.

Mode of Action of Ionizing Radiation

While no attempt can be made to present an account of the effect of ionization radiations on tissue, it must be realized that little of the lethal damage to the malignant cells is caused by a "direct" action of the radiation on the internal cell structures. A certain proportion of cell nuclei are destroyed by a direct hit from an ion, caused by the radiation, but much of the damage is done by what is known as the "indirect" action of the radiation. Biochemical changes are caused in the tumour which so interfere with the metabolism of the neoplastic cells that their survival is imperilled. This indirect action of radiation depends also on a tumour bed capable of playing its part in the destruction of damaged neoplastic cells and providing the mechanism for subsequent tissue repair; the tumour bed must therefore not be so greatly damaged by the applied radiation that it is incapable of recovering its functions.

(1) Tissue of Origin and Site of Neoplasm

Certain sites in the body are particularly favourable for radiation therapy, and the cure-rates which ensue are better overall than can be obtained by surgical methods, and are high in the less advanced cases. These sites are mouth, lip, skin, and bladder. The first three are all accessible for radiation treatment, and the early or moderately advanced primary can be accurately defined and treated with adequate margin. In the bladder, the neoplasm can be made accessible at operation and the results in early lesions are excellent. In another group, the pharynx and larynx, radiotherapy while not offering an exceptionally high cure rate, is preferable to surgery because the latter involves disproportionate risk, or causes grave dysfunction without at the same time providing a higher chance of cure.

Surgery holds first place as the method of treatment of carcinoma in the stomach, small and large intestine, gall bladder, and pancreas, and in all these sites radiation is of no value. Surgery should also be employed, where possible, in malignant growths of the œsophagus, lung, rectum, anus, penis, and scrotum, and in the majority of intracranial tumours; but radiotherapy may be employed in all these sites as an alternative to surgery.

The group which should be dealt with by a planned attack of surgery and radiotherapy combined, is a large one. It comprises, in the main, all those sites in which surgery alone, or radiotherapy alone, is capable of curing a fair proportion, but in which recurrence is to be expected for the majority. The proportion cured by one or the other method is to some extent made up from different individuals, and so the use of the two methods in sequence provides a higher cure rate than either alone. There is evidence also that malignant cells in small clumps or strands are more easily destroyed by radiation than when forming a definite tumour, and this also affords a rationalization of the combined approach. Carcinomas of the breast, thyroid, parotid, nasal sinuses, kidney, and testis, all fall into the group best treated by the combined method.

(2) Degree of Advancement

In the primary site this factor usually directs the choice of treatment method towards radiotherapy, principally because the spread of neoplasm across tissue boundaries or fascial planes militates more against surgical success than against effective radiotherapy. Large primaries, also, may leave gross deformity or loss of function if excised with the necessary margin, and although these factors are of secondary consideration in the curative treatment of cancer, radiation may be preferred when there is otherwise nothing to choose between the two alternatives. There is often surprising reconstruction of the invaded tissues after successful radiation treatment. Small primaries in difficult sites for surgery may also be judged more suited to radiation treatment.

Lymphatic metastases, if from a well-differentiated primary tumour, are usually a field for surgery, provided a planned removal of all the invaded chain of lymph nodes can be undertaken This is the case even though the primary site is one which is best dealt with by radiation. In less well-differentiated carcinoma it is generally advisable to rely on radiation for both primary and lymph node spread.

Radiation is practically invariably used for distant metastases, but there is a small field for surgery, which should not be forgotten, in those neoplasms which are prone to produce solitary distant secondaries

have a thin-walled metal face which permits their passage; the gamma radiation is still present, but its intensity is of a lower order of magnitude than the beta radiation, and may practically be ignored in this special connection. Radium has a half life of 1730 years, and its intensity of radiation may therefore be regarded as constant.

The first daughter element of radium is the gas radon. It has a half life of rather under 4 days, and may be separated from its parent and sealed into very tiny sources known as radon seeds, usually made of gold. Seeds may be permanently or temporarily implanted into tissue, and exhibit their gamma ray activity over a limited period of time and with a diminishing intensity. Appropriate account must be made when calculations of gamma dosage from radon are made, to allow for its rapid decay.

The artificial radio-elements, which are used therapeutically, may emit either beta particles only, or gamma rays only, or both beta and gamma radiation, and their half lives vary from a few days to a few decades. That radio-element is selected for use which emits the radiation of the type and energy required, and which has the appropriate half-life. Radiocobalt (symbol: 60 Co; half-life 5·3 years), Iridium (192 Ir, 70 days), Cæsium (137 Cs, 33 years), Tantalum (182 Ta, 120 days), Gold (198 Au, 2·8 days), Strontium (90 Sr, 25 years), Iodine (131 I, 8 days), Phosphorus (32 P, 14·3 days), are the principal radioisotopes which are being used, or are being considered for use today. Many other radio-elements have been used in tracer quantities in physiological or pathological research.

Conventional X-ray machines work in the range from 60 kV. to 500 kV., and the radiation is used for superficial penetration at the low energy end, and deep penetration at the high energy end of the range. Many devices are employed to ensure accuracy of direction of the beam and delivery of the desired dose.

Radium and the artificial radio-elements whose energy range is from 500 kV. to 2 MeV., are more flexible than X-ray tubes. They may be implanted directly into the body as needles, tubes, or seeds, and there exert their ionizing action locally over a precisely limited area, with little spread of radiation beyond. They may be held at a short distance (½–3 cm.) from the skin or mucosa on applicators constructed for the purpose from wax, rubber, or plastics, known as moulds, which, following the contours of surfaces accurately, can deliver calculable dosage to such surfaces without irradiating the underlying tissue heavily.

When held at a greater distance from the surface (5–15 cm.) the necessarily large amount of radioactive substance (equivalent to 5–10 gm. of radium) must be contained in a heavy metal shield both to define the beam of radiation and to prevent unwanted radiation reaching the patient or others in the vicinity. This is the principle of the radium bomb (or beam), more usually known now as a telecurie unit. Because of the greater distance between the radiating substance and the skin, an increased proportion of the radiation reaches the underlying tissues. An X-ray machine to produce radiation of the same energy would, by its very size, have to operate at a much greater distance from the treated surface, and this would make the proportion of the incident radiation reaching deep tissues very great. For all these purposes radium is in general use, though radio-cobalt (60 Co) is also now being employed, especially for the telecurie units.

By removal of the radiation source still further from the skin surface (40–100 cm.) the same effect is produced as of an X-ray machine working at this energy. A very large quantity of radioactive material (250–2,000 curies), equivalent to 250–2,000 gm. of

The different tissues of the body are damaged by radiation in different degrees, and neoplastic cells are in general more readily damaged than normal cells, and recover from the damage less readily. It should thus be possible to find the right radiation dose which will cause, directly or indirectly, lethal damage to all the cancer cells, whilst allowing the normal cells to recover from the radiation damage, and to preserve their function. This is more certainly done if the radiation dose is delivered spread out in time in daily fractions, since a cell is most sensitive to radiation damage when in the early stage of mitosis. The neoplastic cells, which are dividing frequently, are thus very liable to lethal damage whereas the normal cells of the tumour bed, which are in the main resting, are able to preserve their functions of completing the destruction of the neoplasm and repairing the irradiated tissue. Radiation treatments of a curative nature are therefore usually extended over from 3–6 weeks.

The radiation reaction, which must take place if cure is to follow, is seen on the skin as an erythema, and on mucosa as a fibrinous exudation; these phenomena are the visible signs of the biological changes which are taking place in and around the neoplasm. They must be recognized as an integral part of a curative radiotherapeutic treatment.

The Nature and Production of Ionizing Radiations

The ionizing radiations used for radiotherapy are electro-magnetic waves of the same nature as wireless waves or light, but of much greater energy. As they pass through tissue they yield part or all of their energy, whenever deflected or absorbed, in the form of electrons which cause ionizations in the tissue. These electro-magnetic waves can be produced at different energy levels over a wide range. The greater the energy they possess, the shorter is their wavelength and the greater is their power of penetration into tissues.

The levels of energy of the radiations used in radiotherapy today range from 60,000 volts (60 kV.) to 30,000,000 volts (30 MeV.). The radiations themselves may be produced by electrical methods (X-ray machines), or as the result of atomic disintegration of radioactive elements. It is customary to refer to the machine-made waves as X-rays, whilst those from the radioactive elements are called gamma rays. There is no difference in physical nature between X-rays and gamma rays, and neither does there appear to be any qualitative difference between the biological effects they produce. There are quantitative differences, the most important practical application of which is the particularly high level of ionization caused by low energy radiation as it traverses bone.

The radioactive elements are either naturally occurring, or are artificially made, usually by neutron irradiation in an atomic pile. They undergo spontaneous atomic disintegration, emitting in the process either gamma rays or particulate radiation of several different kinds, or both, the rates of the decay being invariable for each particular radio-element. The time taken for an initial amount of a radio-element to decay to half that amount is known as the half-life, and ranges from hundreds of years to fractions of a second.

Radium is the most important of the naturally occurring radio-elements which are used, and it, together with the daughter radio-elements formed from it by its natural decay, emits alpha, beta, and gamma radiation The metal container in which the radium is sealed, filters or screens off the alpha and beta particles so that it may be regarded solely as a source of gamma radiation. For some purposes beta particles, which also cause ionization in tissue, are required, and plaques containing radium are available that

have a thin-walled metal face which permits their passage; the gamma radiation is still present, but its intensity is of a lower order of magnitude than the beta radiation, and may practically be ignored in this special connection. Radium has a half life of 1730 years, and its intensity of radiation may therefore be regarded as constant.

The first daughter element of radium is the gas radon. It has a half life of rather under 4 days, and may be separated from its parent and sealed into very tiny sources known as radon seeds, usually made of gold. Seeds may be permanently or temporarily implanted into tissue, and exhibit their gamma ray activity over a limited period of time and with a diminishing intensity. Appropriate account must be made when calculations of gamma dosage from radon are made, to allow for its rapid decay.

The artificial radio-elements, which are used therapeutically, may emit either beta particles only, or gamma rays only, or both beta and gamma radiation, and their half lives vary from a few days to a few decades. That radio-element is selected for use which emits the radiation of the type and energy required, and which has the appropriate half-life. Radiocobalt (symbol: 60 Co; half-life 5·3 years), Iridium (192 Ir, 70 days), Cæsium (137 Cs, 33 years), Tantalum (182 Ta, 120 days), Gold (198 Au, 2·8 days), Strontium (90 Sr, 25 years), Iodine (131 I, 8 days), Phosphorus (32 P, 14·3 days), are the principal radioisotopes which are being used, or are being considered for use today. Many other radio-elements have been used in tracer quantities in physiological or pathological research.

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radium, is needed to produce a high enough dose-rate for practical use and this rules out the use of radium, which is not plentiful enough and which occupies too great a volume. Sufficient quantities of artificial radioactive substances can be manufactured, however, which have very high activity in a small volume, and they may be used for this purpose; those most likely to be so employed are cobalt (60 Co) and cæsium (137 Cs). Their advantage over the X-ray machine producing radiation of this energy will be freedom from breakdown and low cost of maintenance.

Other radio-elements used are iodine (131 I) and phosphorus (32 P) which are given by mouth or intravenously, for specific purposes, and gold (198 Au) which is used in colloidal form in the pleural or peritoneal spaces, or in solid form to replace radon seeds. Strontium (90 Sr) and phosphorus (32 P), which are beta emitters, may be used for the treatment of superficial lesions.

Above the energy level of the gamma rays from radium and the new artificial radio-elements, electrical machines of non-conventional type are now capable of being constructed to produce X-rays at from 2–30 MeV. Van der Graaf Generators at about 2 MeV., and linear accelerators from 2–15 MeV. or more, have been built and some clinical work done. Betatrons and synchrotrons up to 30 MeV. or higher are also being explored as therapeutic weapons. It seems safe to prophesy that up to 4 or 5 MeV., the technical advantages obtainable should lead to greater effectiveness in the treatment of malignant disease, but above this energy level the value of these large and expensive machines is questionable, unless some unexpectedly different biological effect of the radiation they produce is observed.

Tumours of the Skin

Basal celled carcinomas are usually treated with superficial X-rays if they are not excessively large, and are on relatively flat surfaces. On much curved surfaces as in the inner canthus of the eye, or the bridge of the nose, they are more exactly and successfully dealt with by surface moulds of radium or radon, or by radium and radon seed implants. They are radiosensitive but show considerable variation in response, though it is rare to find a truly resistant example. Radiation failures are best excised, as second treatments are often followed by late necrosis.

Squamous celled carcinomas are generally more resistant than the basal celled variety, and a high local dose is necessary. Radium methods, either mould or implant, are therefore preferable to X-rays, unless the lesion is small. A full centimetre of healthy margin must always be treated.

In very large primaries, whether basal or squamous, a determined initial attempt at cure must be made, as if subsequent recurrence take place ultimate cure becomes unlikely. Radium methods are preferable to X-rays, and teleradium is probably the method of choice, especially if bone is involved. Subsequent surgery, to remove devitalized bone and tissue is often advisable, and plastic repair and the construction of prostheses play their part.

There are certain sites where surgery may be preferable to radiation. On the pinna, the incidence of radionecrosis of cartilage is high, and this factor in conjunction with the technical difficulties of radiotherapy in the site, make partial amputation of the pinna a more satisfactory alternative in many cases.

On the limbs, and particularly on hands and feet, the liability to radionecrosis is also

high, especially in the elderly, and although small lesions are reasonably safe and curable, larger lesions, notably on the dorsum of the hand or foot give rise to difficulty. A high dose will cause necrosis but a lowering of this dose to a safe level will result in many failures to cure. The same considerations apply to epitheliomas of the arms or legs which involve more than two-thirds of the limb circumference. A surgical attack on these lesions is therefore indicated, but if this necessitates amputation then a radium mould should be used as a first attempt, leaving amputation in reserve. It should not be overlooked that delay in curing the primary increases the likelihood of lymphatic metastasis.

Squamous carcinoma arising on lupus is less commonly seen now that skin tuberculosis is more effectively treatable, and it responds well to radium mould methods. Epithelioma arising on previously irradicated skin should be excised.

The premalignant keratoses that occur on exposed skin in the elderly, and on the hands and arms of oil and tar workers (pitch warts) are simply treated by superficial X-rays or by beta particle applicators. Intraepidermal carcinoma (Bowen's disease) is also very responsive to superficial X-rays.

As with carcinoma in any site, lymph node metastasis reduces the probability of cure to about one-third of that in the uncomplicated case. These secondaries, probably because of the different tumour bed in which the malignant cells are growing, are rarely curable by radiation, and surgery is the preferable method of dealing with them. Formal block dissection with the most careful and scrupulous technique is demanded, and will be found to give rewarding results. If inoperable, or if age or concomitant medical conditions prevent surgery, then radiation can be employed as a palliative measure. If primary and secondaries are present at the same time, there is no contraindication to using radiation for the one and surgery for the other.

Malignant melanoma (melanocarcinoma) is in the opinion of the majority best dealt with by very wide and deep excision. Although some may be radiosensitive, this does not appear to be sufficiently common to justify the adoption of radiotherapy as the primary treatment method. In any event, the long term results of both surgery and radiation are not good, and a rational approach would appear to be preliminary irradiation to full dose, followed by radical excision. Operable lymph node metastases may also be dealt with by the same combined method; radiation alone is certainly rarely effective. There are unfortunately many pigmented skin lesions which it is not possible to diagnose with certainty on sight, and biopsy is held, with considerable justification, to be a cause of early metastasis in malignant melanoma. If a lesion is clearly a malignant melanoma, it should not be biopsied; doubtful lesions may be biopsied immediately after a preliminary irradiation.

The rarer skin malignancies of a glandular character, such as epithelioma adenoides cysticum are radio-resistant and better excised. Papillomas may be treated by radiation, if in awkward sites, but it is a mistake to imagine that because they are benign they require a lower dose; the reverse is the case. Skin fibromas and "moles" are quite unaffected by any safe dose of radiation. Infective warts are sensitive, but because of their multiple nature and their site on hands and feet, radiation is used only if all other methods have failed, and retreatment must never be attempted.

Keloid scars can be flattened, paled, and rendered less irritable by moderate dosage of radiation, especially if the hypertrophic tissue is young. In plastic surgery, keloid formation can be prevented by irradiation of the skin prior to the incision, and again of

the scar after the stitches are out. Spontaneously arising keloids have a much greater degree of resistance.

Angiomas in children are *frequently treated by radiation if growing rapidly or causing* disfigurement, and an initial rapid regression can be caused, which may be of great value. The ultimate time of disappearance is little different from that which occurs naturally as the child grows older. Cavernous nævi and port wine stains cannot be improved to any marked degree.

Carcinoma of the Mouth and Lip

Carcinoma of the tongue, floor of mouth, and buccal mucosa are all best treated by a radium implant method, and the feasibility of this principally depends upon the extent of the primary growth. Almost without exception, any operable growth can be implanted with good chance of success and many inoperable lesions are quite easily treatable. The implants are done with radium needles, individually stitched in place, and arranged according to well-defined patterns of single plane, multi-plane, or volume type. The positioning of the needles is a matter of great exactitude, and can only be done with a good basic knowledge of radiation physics, and much practical experience. Endotracheal anæsthesia and packing off of the pharynx is an essential preliminary to precision in the placing of the needles.

An alternative method for the floor of the mouth, or for some lesions of the cheek is the use of the intra-oral radium mould. Radium sources are arrayed on special individually-made plastic or composition applicators which fit precisely in place and provide a homogeneous zone of radiation. If the lesions are particularly thick, the intra-oral mould must be reinforced by another mould supported externally, so sandwiching the lesion.

Telecurie methods are also especially applicable to mouth lesions, but of necessity more surrounding healthy tissue is irradiated, and the radiation reaction is therefore more severe for the patient. The treatment course is also long drawn out, and the majority of radiotherapists prefer implants or moulds. For larger lesions that cannot be accurately implanted or moulded, telecurietherapy becomes the treatment of choice, being in its turn less severe than any X-ray method. If bone is involved, or is in very close proximity to the growth, then telecurietherapy or a mould is always preferable, since the risk of production of bone necrosis is rendered minimal. X-rays in the conventional range, and radium implants close to bone, are very liable to produce this complication.

Late bone radio-necrosis is usually precipitated by infection, access being gained by the organisms through a breach in the irradiated mucosa. The commonest cause of such a breach is dental extraction. It is therefore advisable to extract all teeth that will come within the highly dosed zone, whether faulty or perfect, before treatment starts. If this has not been done, then dental conservation after irradiation should be carefully practised, and extraction avoided. If the latter becomes inevitable it is best done under full antibiotic cover. Bone necrosis is more common and more severe in the mandible than in the maxilla, and may occur many years after the radiation. In the treatment of radiation bone necrosis it has been the practice in the past to await sequestration, which usually takes many months. With the advent of intensive antibiotic therapy, it is now possible to remove the infected bone widely and to obtain subsequent healing, thereby saving the patient much suffering; modern practice therefore is to advise early resection

of all the involved bone, as soon as it is clear that simple measures have not been successful.

Syphilis is, in general, a contraindication to radiation therapy in the mouth. Owing to the diseased blood vessels and pathological stroma, an adequate tumour bed response does not occur and recurrence or soft tissue necrosis is a very common sequel. While small lesions may be treated, leaving surgery in reserve for the not improbable failure, larger carcinomas are best dealt with by radical excision.

Leukoplakia may be dealt with by radiation, but in the opinion of most, this is rather dangerous practice; attention is better directed to possible areas of malignant change rather than to the leukoplakia itself. Raised roughened lesions frequently show premalignant downgrowth, but the flat translucent lesions rarely do so. It is advisable to treat each malignant area as it arises with a limited radium method, and for this purpose radon seeds are very suitable. Seeds are, indeed, suitable in the very elderly patient as a treatment method for any malignant mouth lesion of limited size. They may be implanted under local anæsthesia, and hospitalization so avoided.

Carcinoma of the fauces, or tonsillar region is difficult to implant satisfactorily as it frequently involves soft palate and tongue by extension. X-rays or telecurietherapy can be used in this site with considerable success. Lymphosarcoma or reticulosarcoma of the tonsil is dealt with by X-rays, treating the cervical lymph nodes at the same time.

Carcinoma of the palate is difficult to deal with, except by an intra-oral radium mould. If it is spreading backwards on to the soft palate where a mould cannot be tolerated, a radon seed implant is the best alternative. Care must be taken to ensure that the lesion in the mouth is not also involving the floor of the nose. If such be the case treatment should be conducted on the lines suitable for a carcinoma in the nasal cavity.

Carcinoma of the lower lip is curable in high proportion, by any of several radiation methods. Superficial X-rays, if necessary applied both to the skin and the mucosal surfaces, is suitable for small lesions, or moderate sized ones in elderly patients. Double radium moulds of sandwich type are the most exact, though difficult technically to produce, and give very good cosmetic results. Radium implants are equally successful. Small differences in extent and thickness of the growth may be a deciding factor in which method shall be employed. The rare upper lip lesion is much more dangerous, both from the viewpoint of rapid spread and of lymphatic metastasis, and must therefore be treated urgently and with wide margin. This is particularly true of lesions at the angle of the mouth.

The presence of invaded cervical nodes, or their appearance subsequent to treatment of the primary oral carcinoma, is of grave prognostic importance, since it reduces the cure rate by a very large factor. The accepted method of treatment is by block dissection but the results are critically dependent on the technical skill with which the operation is performed. It must be done as early as possible, and in the case presenting with a primary mouth carcinoma and secondary nodes present, is best done as soon as the treatment for the primary is completed, and without waiting for the radiation reaction to subside.

In the "node free" case, frequent follow-up is vital, as nodes may appear at any time in the first year after treatment of the primary, and occasionally even later. Monthly follow-up is therefore advisable, and the all too common practice of 3 or even 6 monthly follow-up cannot be too strongly deprecated. As soon as nodes become apparent the block dissection should be undertaken, without waiting for clinical certainty. A few cases

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operated upon, but subsequently shown histologically not to have in fact had malignant nodes should not allow this policy to be varied.

Carcinoma of the Nasal Sinuses

Carcinoma in the maxillary antrum, when arising in the lower part, is potentially curable by the simple insertion of a radium tube through the upper alveolo-buccal sulcus into the growth. The lateral wall of the cavity, in this region, is usually invaded and a malignant ulcer in the sulcus is frequently the symptom that first brings the patient to treatment. The radium tube can generally be introduced by direct pressure straight through the neoplasm and the softened bone, though it may be necessary to incise the mucosa and break through the antral wall. Preliminary removal of tumour tissue is inadvisable. The success of this type of treatment is dependent upon the situation of the growth, which in invading the lateral wall very early creates the situation of an accessible carcinoma of relatively small size. The stoma formed at the insertion often closes and it may later become necessary to drain the cavity by a palatal antrostomy; it is perhaps surprising that this procedure is comparatively seldom needed.

An alternative to the above procedure, which is applicable also to more extensive growths, is the external use of telecurietherapy or X-rays, the former being preferable. After the resulting radiation reaction has settled, a palatal antrostomy is performed and necrotic tissue and bone are removed. If malignant tissue is found, it is removed as completely as possible, following the cancer to its limits; into the cavity thus created a radium mould is inserted, and the walls of the cavity are irradiated again. If no neoplasm has been found at operation, then the radium mould treatment is omitted by some.

This principle of treatment is in theory applicable to even very advanced malignancy, providing glandular metastasis has not occurred; it may be necessary to sacrifice the eye, if the orbital plate has been invaded, or to remove the medial wall and create a large cavity communicating with the nose. Naturally the more extensive the neoplasm, the more extensive is the irradiated zone, and the more extensive is the surgical procedure. In very advanced neoplasms, where the soft tissues of the cheek have been invaded, or the pterygoid fossa involved, it is probably advisable to rely on the preliminary external radiation alone, as the extensive and disfiguring surgery necessary is not warranted, since cure is very remote.

Carcinoma of the ethmoids is generally extensive before it is diagnosed, and is moreover inaccessible. Various radium implant methods have been tried but have proved unsuccessful. External treatment by a telecurie unit is advisable.

Carcinoma in the nasal cavity is generally extensive, often with much sub-mucosal spread, the limits of which are difficult to determine. Intra-nasal radium tubes or telecurietheraphy can deal satisfactorily with tumours of limited extent, but for more extensive growth it may be necessary to resect the palate, septum, and turbinates, creating a large central cavity which can be irradiated by a radium mould inserted from below.

Carcinomas of the middle ear are often locally advanced before the diagnosis is made, with spread of indeterminable extent in the temporal bone. Telecurietherapy is the treatment of choice, and subsequent surgery for the provision of drainage, or the removal of necrotic bone fragments is often required. Radiation effects on the brain stem, which is in close relationship to the diseased area, is a danger which can partly be obviated by the use of good radiotherapy planning. The true middle ear carcinoma has a bad prognosis,

but is a rare condition. Many of the reported good radiation results come from carcinoma of the auditory meatus arising originally in skin, and of comparatively limited extent. They are technically difficult to treat but not insuperably so, and a high proportion of radiation cures should be obtained.

Secondary neck nodes from all this group of carcinomas are of late occurrence, and are usually associated with extensive growths of undifferentiated type; block dissection is not called for. The presence of secondary glands therefore usually determines that extensive radical procedures, for the primary tumour are not indicated, and radiation palliation is all that is advisable. Lymphosarcomata of the upper jaw, which may give rise to neck nodes early, should be treated by external irradiation methods, and surgery has little part to play

Very close co-operation is called for between surgeon and radiotherapist in the handling of patients suffering from carcinomas in these sites. It is also necessary to obtain help from the dental laboratories to construct the temporary or permanent prosthesis needed at different stages of treatment. In spite of all efforts, the number of cures in this group is very low, except for the lower pole antral carcinoma already mentioned. Local disease usually persists, and since lymphatic or blood borne metastases are uncommon, the patients survive suffering from pain due to local growth, sepsis, or sequestrating bone, often for many years. The more widespread use of high energy radiation gives a hope that in the future we may be able to do more for this unfortunate group than in the past.

Carcinoma of Larynx and Pharynx and Cervical Glands

Radiation holds its place as the primary method of treatment for cancer of the larynx, mainly because of the gross functional disablement caused by laryngectomy. There is little reason to doubt that were all sufferers subjected to the complete radical operation, the cure rate would be higher than anything that has so far been achieved. The successes of radiotherapy, as for all cancer therapy, are greatest in the small localized lesion. When strictly confined to the anterior two-thirds of one vocal fold, but not involving the commissure, the use of a radium implant, by the well tried Finzi-Harmer technique, or by a variant of it, provides the most successful approach. This method has tended to fall into disuse with the increasing use of teleradium, and has also suffered because of unsuccessful attempts to utilize it for more extensive lesions; but it is less arduous for the patient than a long teleradium course with its attendant radiation reaction, and is preferable, since the cure rate cannot be bettered. It is strongly emphasized that the indications for its use must be most rigidly adhered to.

Telecurietherapy is applicable both to the very early and to the more advanced lesion, though for maximum success it would seem that a high dose delivered over a period of 5 or 6 weeks is necessary. Most lesions, if confined to the endolarynx, show good results by this method in the first 2 or 3 years but the number of recurrences is disappointingly high, and the 5 year cure rate is only impressive in the early lesions. X-ray therapy at ordinary kilovoltages produces a cure rate of the same order of significance, statistically, as does the telecurietherapy, but is not generally preferred owing to the greater liability to post-irradiation laryngeal œdema and to cartilage necrosis. Disease of the arytenoid region or aryepiglottic fold, whether primary or by extension from the endolarynx worsens the prognosis, as does muscle infiltration giving rise to defective cord movement With subglottic extension, or involvement of thyroid cartilage, or

spread into the pyriform fossa the prognosis is so poor that laryngectomy should be seriously considered as the primary method of treatment.

In the pharynx, the methods of radiation employed are telecurietherapy or X-ray therapy, but except in the early lesion without lymph node spread, the results are disappointing. There has been a recent revival in interest in a surgical attack on these neoplasms, largely because of the poor radiation results, and it remains to be seen what improvement may be obtained, and whether criteria can be established for the selection of cases for one or other method to give an improved cure rate.

When lymph nodes become involved subsequent to an initially successful radiation attack on a primary in larynx or pharynx, the block dissection operation does not provide a solution as satisfactory as in carcinoma of the mouth. X-ray treatment of these nodes is also often rendered difficult, if not impossible, by the previous treatment already given to the primary. There is therefore a good case for the inclusion of the lymph node chain in the treatment fields for a primary lesion even in the absence of their clinical involvement, except in early endolaryngeal growths where subsequent lymph node spread is improbable.

Nasopharyngeal carcinoma presents a rather different problem as curative surgery in this site is impracticable, and radiation methods vary according to the histology of the growth. With well-differentiated squamous carcinoma, X-ray therapy with small fields, or radiation from a radium source placed in the nasopharynx, or a combination of both are the methods employed. The creation of a large stoma through the soft palate is an aid to the radium treatment, and is of value to provide easy subsequent inspection. With anaplastic growths, or "lymphoepithelioma" or lymphosarcomatous lesions, wide field X-ray therapy is employed, since spread to cervical lymph nodes or up to the base of the skull, giving rise to cranial nerve palsies, is of early occurrence. Results are initially good, but long term cure rate is low.

Neoplasms of the Parotid, Thyroid, and Neck

Carcinoma of the parotid presents a special problem. It is difficult to determine the extent of disease in the gland and the character of the neoplasm makes it extremely unlikely that cure of the growth will follow irradiation of the whole of the gland. The anatomy of the part renders total parotidectomy a formidable proceeding and any lesser operation can hardly satisfy the principles underlying the successful surgical treatment of malignancy. Surgical removal is therefore advisable followed by radiotherapy. If the lesion has been comparatively superficial, the latter should be by a radium implant which will deliver a high local dose to any residual cells. If more extensive, then a radium implant is impracticable and X-ray or telecurietherapy must be used, though with a more limited likelihood of success. In lesions too advanced for surgery, radical X-ray therapy should be employed but the results are poor except in some unusually sensitive types mostly found in elderly patients.

In the past mixed parotid tumours were excised by simple enucleation, and a subsequent radium implant was found markedly to reduce the incidence of recurrence. At the present time many surgeons are performing parotidectomy with dissection of the facial nerve for this condition, and radiation is being less frequently used as a supplement, though it would still seem a useful precaution to insert a radium implant at the conclusion of the operation. Salivary tumours in the oral cavity should be treated in the same way.

Lymphosarcoma of the parotid region is primarily best treated by X-rays, including the associated chain of lymph nodes, whether clinically involved or not. The rare adenolymphoma does not need radiation treatment subsequent to excision, as there is little tendency to recurrence.

/ Parotid fistulæ heal readily if the affected gland is given a small dose of X-rays, sufficient to dry up its secretion for a short time.

For carcinoma of the thyroid, the accepted principles of treatment are initial surgery of the primary and involved lymph nodes followed by X-ray therapy. Neither method separately used is highly successful, but give improved results in combination both for advanced primary growths or for small localized lesions such as malignant adenomas. In the former cases, surgical extirpation, if at all practicable, is advisable even though clear technical operability is doubtful, and in the latter post-operative irradiation should be used even if the surgical clearance seems to have been excellent. The better results are, of course, obtained when the neoplasm is of a highly differentiated character. With very anaplastic carcinomas, local cure can occasionally be obtained by X-ray therapy alone, as radiosensitivity is often well marked. Retrosternal extension of a primary should be removed if possible with the initial surgery, and the area and mediastinal lymph nodes subsequently irradiated. Bone metastases from thyroid carcinomas are sometimes solitary and X-ray therapy can be energetically used, as long term survival may be obtained.

Lymphosarcoma should be treated by radiation alone and Hashimoto's Disease and Riedel's thyroiditis respond well.

Radioactive iodine therapy for thyroid carcinoma is arousing widespread interest and a number of remarkable results have been obtained. The isotope (131 I) is specifically metabolized in the thyroid gland, and the beta and gamma radiation emitted act from within the cells that contain it. The normal thyroid gland takes up the radio-iodine that has been administered by mouth to a much greater degree than a thyroid neoplasm which, indeed, usually does not take it up at all. Preliminary experiment is therefore done with minute amounts (tracer doses) to see if the neoplasm is a functioning one. It is not easy to determine this, as the adjacent normal gland takes up to such an extent that physical methods cannot easily distinguish between the gland and the tumour.

The highly differentiated adenocarcinoma is the growth most likely to absorb the isotope, and an anaplastic carcinoma is certain not to do so at all. Biopsy specimens of the tumour, examined by autoradiography, and by direct measurement of radiation may help to establish the degree of tumour uptake. If any indication is found that the neoplasm can absorb iodine, there is a reasonable hope that if the competition of the normal gland for it can be removed, the tumour will then take up sufficient for a curative attempt to be made. The normal gland, and as much of the neoplasm as possible are accordingly removed surgically, or a sufficiently large dose of radio-iodine is given to destroy the normal gland by its radiation. Subsequent tracer studies will then show whether residual tumour, or metastases, have become capable of picking up iodine to a great enough degree for therapeutic dosage to be administered. The procedure, as outlined only here, is one calling for highly specialized knowledge and equipment and should not be attempted without full laboratory facilities and a trained physicist staff.

The method is still in process of development, but the present indications suggest that standard surgical and radiotherapeutic measures, coupled with tracer studies to determine possibility of iodine uptake, should be used for the primary tumour. In the

light of the tracer results, investigation and treatment for local recurrence or for distant metastases can then be carried out. The results of radio-iodine therapy in patients who have had a functioning tumour are most promising, even when widespread metastases are present.

Hyperthyroidism can be treated by radio-iodine, as will have already been realized, since the thyroid gland selectively absorbs this element and cannot distinguish between it and its non-radioactive isotope. Following tracer studies, an estimate of the amount necessary to reduce the high level of function to normal can be made. After administration, improvement follows in 6 weeks to 3 months, and further dosage can be administered as is required.

Contraindications to this type of treatment are adenamatous glands, and long standing goitres which have become toxic. Young subjects should not be treated, because mutations may occur in the germ-cells of the gonads, due to a small proportion of radiation that the whole body inevitably receives, and in the female particularly because the ovaries receive irradiation as the iodine is excreted in the urine. The subsequent occurrence of malignant change in the irradiated thyroid has been offered as an objection to radio-iodine therapy, but little evidence can be found to suggest that this is more than theoretical. Particular indications for treatment are the failed surgical and anti-thyroid drug cases, and those with progressive exophthalmos. In the past, X-rays have been much used for hyperthyroidism but with radio-iodine and anti-thyroid drugs now available, there seems little indication for the continuance of this.

Carcinoma in neck nodes, secondary to an undiscovered primary, is a common clinical picture, and X-ray therapy as a palliative agent may be used. The majority of the primary growths are small ones in the bronchus, but kidney and ovary should not be overlooked in the search. Tiny submucous growths of pyriform fossa, or nasopharynx, may also produce large malignant neck nodes.

Tuberculous glands of the neck respond very favourably to long continued low dosage X-radiation, and judicious treatment can prevent threatened breakdown and avoid operation. Actinomycosis of face or neck, if not readily healed by antibiotics, also provide a field for similar long term low dose therapy, and the results are good. In the thorax and abdomen this disease does not respond so well, but is worth a trial if other means are unsuccessful.

Neoplasms in the Thorax

Carcinoma of the bronchus is very uncommonly cured by radiation, and pneumonectomy, if practicable, is the treatment of choice. In a few patients with small growths, too near the carina for operative removal, or involving the trachea, attempts at radical cure by X-rays are indicated. For the remainder of the inoperable growths, palliative X-ray therapy is advisable for a proportion, but it must be realized that once mediastinal lymph nodes are invaded, cure cannot be obtained and long drawn out debilitating treatment courses are rarely justifiable. The principle value of palliative therapy is in the relief of actual or incipient mediastinal obstruction, and in the relief of pain, hæmoptysis and dyspnœa; all these can usually be affected with moderate dosage.

Treatment with radiation is contraindicated in the elderly and cachectic, in those with bilateral growth, with intrapulmonary metastases, with abscess formation or with malignant effusion; œsophageal involvement and visceral metastases also render treatment

inadvisable. Oat-celled carcinoma, which is considerably more radiosensitive than the other varieties, is often worthy of more serious palliative attempts if confined to the thorax, since extended survival may be obtained. It is possible that there is a primary indication for radiotherapy rather than surgery in the oat-celled tumour.

In post-pneumonectomy patients, irradiation is not indicated if a complete surgical clearance has been possible. Where the primary has been removed but mediastinal glands are known to have been left, it is in general also unwise to give post-operative therapy unless the pathology is of the oat-celled type. X-ray treatment is not well tolerated by the post-pneumonectomy patient, and a sufficient dose to affect adequately the residual mediastinal lymph nodes cannot be safely administered; it is better to wait until symptoms become apparent and then use X-rays palliatively.

Mediastinal tumours which are suitable for radiation therapy are those due to bronchial carcinoma, Hodgkin's disease, lymphosarcoma or allied reticuloses. All these may be treated palliatively. The rarer teratoma, neurofibroma, or fibrosarcoma are not responsive to irradiation. In the case undiagnosable without thoracotomy, a short course of X-ray therapy may indicate the probable diagnosis and determine the future treatment plan. Thymic tumours, if malignant, appear to have some degree of radiosensitivity, and a combination of surgery and radiotherapy is probably advisable. When myasthenia is the presenting symptom, surgery should be undertaken if a tumour is demonstrable, and be followed by X-radiation, but in the absence of a tumour, X-ray therapy alone is often successful in causing remission of the symptoms, though several months' delay before improvement occurs is usual.

Œsophageal carcinoma has been in the past usually treated by X-radiation. Undoubtedly dysphagia can be relieved and life extended in cases initially fit enough for the protracted course of treatment necessary; but the cure rate is very low indeed. In the lower third, the columnar celled growths so often found are not radiosensitive and the site is an unsuitable one for treatment by X-rays, owing to the proximity of the liver and to the thickness of the thorax. Surgery is undoubtedly preferable in this region. In the middle third, radiation provides fair palliation, but if surgery is practicable it should be carried out. In the upper third rather more radiation cures are obtained, and the use of endœsophageal bougies carrying radium, combined with external X-rays or teleradium has had limited success in small post-cricoid neoplasms. Radiation is contraindicated in the elderly and debilitated, and where mediastinal extension is apparent. Gastrostomy as a preliminary to radiation is often of value as it enables the general nutrition of the patient to be maintained.

Carcinoma of the Breast

It has been customary to divide cases of breast cancer into various stages based upon the clinical extent of the disease, and to use this staging as a guide to the method of treatment to be employed. Study of the results obtained from large numbers of cases has led to the realization that extent of disease estimated in this way is only of limited value in relation to prognosis and to treatment method, and that there are other factors, often difficult to assess, which play an equally important role when the treatment policy for a patient is to be decided.

The most important of these other factors is the rate of growth of the tumour, which is naturally closely associated with its histological characteristics. Since the latter cannot

be determined adequately before removal of the primary growth, an attempt must always be made to assess the rate of growth by close questioning of the patient, and by correlating this to the observed physical signs. If evidence is obtained that growth is proceeding rapidly, the emphasis moves away from surgery and towards radiation as the initial treatment method. The physical age of the patient does not, *per se*, appear to be related to the probability of cure, but is of significance in that the younger age groups more commonly suffer from rapidly growing and anaplastic cancers. The patient's menstrual state is of greater significance, since it has been shown in numerous series that cancers arising at, or shortly after, the menopause carry a bad prognosis, whereas in the few years before the menopause the outlook is more favourable.

A different emphasis is also now accorded to some aspects of the clinical extent of the disease, notably in relation to the siting of the neoplasm in the inner half of the breast. Here, the lymphatic drainage to the intrathoracic group of nodes associated with the internal mammary vessels affords a probable route of spread which carries a significantly bad prognosis, and being at present inoperable, radiation must be used to treat this lymph node group when the tumour is in the inner half. It is also now becoming appreciated that unless axillary nodes which are palpably involved are freely mobile and low on the medial axillary wall, their operative removal is hazardously associated with the subsequent occurrence of distant spread.

Some surgeons accordingly hold the view that nodes palpable towards the axillary apex, or an axilla which cannot be certainly palpated owing to obesity, are contra-indications to a radical mastectomy. A more serious view is also taken of attachment to deep fascia over the pectoral muscles, and of skin invasion of any greater degree than minimal attachment over the primary.

A consideration of all these points, and of the statistical evaluation of large groups of patients in the various stages, has led to the conclusion that the radical operation is no longer suitable for the majority of breast cancers. Better results are at present being obtained by reserving it for the very early case, and for the remainder to use a simple mastectomy combined with radiotherapy, or else to use radiotherapy alone. The policies of treatment towards which opinion is trending may be summarized in four groups.

Group A. For slow-growing small neoplasms in the outer half of the breast, without deep fixation, and with no more than minimal skin attachment and with no lymphatic or distant spread, the treatment policy is radical mastectomy. No post-operative radiotherapy need be given if the pathological examination subsequently confirms the preliminary assessment, but if there is spread of neoplastic cells wide of the primary mass, or if lymph nodes are microscopically involved, then a radiotherapeutic course should follow. Some, with justification, would employ subsequent radiotherapy in the young and the menopausal age groups in every event. The cure rate of this group (70–80 per cent at 5 years) probably cannot be bettered by any alternative scheme, and there should be but little diminution of this cure rate at 10 years.

Group B. For inner half tumours without lymph node spread, or for any tumour in the breast with axillary lymph nodes involved, skin infiltration not being wide of the tumour, and deep fixation absent or to fascia only, the treatment policy is simple mastectomy combined with radiotherapy The operation should remove the organ without disturbing deeper structures and the axilla should not be dissected, though lymph nodes lying in close relation to the tail of the breast may be removed.

The question of whether the radiation course should be given pre- or post-operatively is a vexed one, concerning which there are no statistics on large numbers of patients available. Post-operative radiation is usual, but there is good reason for using it pre-operatively where there is evidence of rapid tumour growth, or where skin involvement is extensive enough to raise doubts of adequate margin of healthy skin being easily obtainable. The cure rate of this group, at 5 years, should be in the region of 40 per cent, but probably one quarter of these survivors will die in the next quinquennium.

Group C. Cases with more advanced primaries and lymphatic spread than in Group B, but without evidence of blood borne metastases, should be treated initially with radiation and the result observed. In a certain proportion, resolution will be obtained of all except the primary growth, and if this is apparently static then a simple mastectomy may be performed. The operation should, in general, not be undertaken if radiotherapy does not successfully arrest the disease process. A 20 per cent 5 year cure rate may be hoped for, but this will fall very considerably, to 10 per cent or less, in the subsequent 5 year period.

Group D. For cases with blood borne metastases, radiotherapeutic treatment only is indicated, designed to alleviate the symptoms caused by the primary or the metastases. Much can be done by judicious radiation therapy for this group, and those with multiple secondaries in the pelvic bones or spine can often be kept reasonably comfortable for some years. Spread to the lungs or abdominal viscera are contra-indications to treatment except for short palliative exposures to co-existing painful bone metastases. Cerebral metastases rarely repay serious radiotherapy.

The radiotherapeutic method employed in Groups B and C is treatment by X-rays of the breast, or chest wall if post-operatively, including the axillary, supraclavicular, and internal mammary lymph node areas. A brisk radiation erythema just short of the point of moist desquamation is aimed at, and unless such an erythema is obtained, the biological action of the X-rays will not have reached its maximum effectiveness. Subsequent telangiectasia of the area will appear in a moderate proportion of cases. Radiation treatment also will increase the number of those who get lymphœdema of the arm subsequent to surgery, but it is only when used in combination with a radical mastectomy that this complication is common.

With modern techniques, lung fibrosis does not occur, though pleural thickening can often be detected but rarely causes symptoms. Irradiation osteitis of the upper three ribs is also seen on occasion, sometimes with fracture; symptoms are rare, and the appearances must not be interpreted as due to bone secondaries. Radium is seldom used in the routine treatment of breast cancer, but moulds of the chest wall or radium implants are of value in special cases, particularly those of recurrence in the flaps without glandular spread.

No description of the treatment of breast cancer would be complete without reference to hormone therapy. It has been shown that the rate of growth of some breast cancers can be altered by changing the hormonal background of the patient. Sterilization of the pre-menopausal patient, either by ovariectomy or by irradiation of the ovaries, has been advocated for many years, although the statistical evidence for the value of this procedure has not been very striking. The administration of œstrogens to the elderly has been followed in many instances by marked regression of both primary and metastatic growth. In patients who have not reached the menopause or who have only recently experienced it, œstrogens may however cause an increase in the rate of growth of their disease.

More recently the giving of androgens has been shown to have the effect of slowing of the growth, or even causing regression and healing, in relieving the pain of bone metastases and of causing their re-ossification, and in improving anæmia and cachexia. About one-third of these treated show marked benefit, and this has been most evident in the pre-menopausal ages. Some post-menopausal patients have also been helped, particularly when bone secondaries are present. Since the advent of orally active compounds, the androgens can be given as tablets to be allowed to dissolve in the mouth, and a dose of from 50–100 mgm. of methyl testosterone may be given daily. Full effect will not usually be obtained until clinical evidence of masculinization is present. The feeling of well-being induced by the drug is of great value, and most patients obtain an improved appetite and gain weight.

The mode of action, as far as it is at present known, is that the output of endogenous œstrogens is reduced by the administration of androgens, probably because of an effect of the latter on the anterior pituitary. Since the ovary is, in the normal, the principal organ of supply of œstrogens, castration is advisable in patients younger than 7–10 years post-menopausal, if androgen therapy is to be instituted.

The adrenal glands are also a potential source of endogenous œstrogens, and may serve this function in the individual who has had ovaries removed and in spite of androgen administration. Adrenalectomy was thus the natural step to take for the patient whose breast cancer was otherwise uncontrollable, and since the introduction of cortisone has become a relatively safe procedure. About one half of the patients so operated upon have obtained worthwhile regression of growth and relief of symptoms, some to a very marked degree and in a quite spectacular manner. It would appear that their life has been significantly extended.

The next logical step, since endogenous œstrogen output is apparently under the hormonal control of the anterior pituitary, was ablation of the hypophysis. The operation has been followed by the expected regression of growth and relief of symptoms, and it is being claimed that a greater proportion of the patients so treated receive benefit than with the comparable operation of adrenalectomy. Some recent experiments have suggested that an anterior pituitary hormone may have a direct effect on the rate of growth of breast cancer, independently of the hormonal control of the production of œstrogens from the ovary or the adrenal.

It is far too early to attempt to lay down a policy which might be followed for patients with breast cancer uncontrolled by surgical or radiotherapeutic measures. A possible line is ovariectomy (in the younger group of patients), followed by testerone therapy. When the latter ceases to have beneficial effect, then adrenalectomy or hypophysectomy should follow. There are some indications that hypophysectomy may come to be the decisive step, without having to do adrenalectomy at all. The great need is for the establishment of some criterion whereby the likely response to these radical procedures can be estimated beforehand. If a series of biochemical tests can be devised that will provide this need, then the procedures could be undertaken on patients before their disease became too greatly advanced.

The value of œstrogen administration in the elderly should not be forgotten—the older the patient the more likely it is to have a good effect. It is wise to start with a small dose of the order of 1·0 mgm. of stilbœstrol daily, and to increase the dose slowly until an effect is apparent. Up to 15 mgm. a day can be tolerated by many if the dose is not

increased too rapidly, and some patients need that amount, though an effect will be obtained with most at a lower dose.

Neoplasms in the Urogenital Tract

Carcinoma of the kidney, whether of the parenchyma or the renal pelvis is treated by surgical methods primarily. Recent work has suggested that post-operative irradiation of the operation area and adjacent lumbar glands is capable of creating significant improvement in the numbers of survivors, and the adoption of this course is accordingly advisable. In operable growths, palliation can be achieved, but radiation cure is remote. X-ray therapy may, on occasion, convert an inoperable neoplasm into a removable one. Distant metastases may be palliated and sometimes cured locally by X-ray therapy, and if solitary, as is often the case, a curative policy for primary and metastasis should be followed. Many extended apparent cures have been so obtained.

Embryonal carcinoma (Wilm's Tumour) is, in contradistinction to the other renal malignant neoplasms, a radiosensitive growth. Radiation treatment should always be combined with surgery, though opinions are divided between pre- and post-operative X-ray therapy. The treatment fields should always be large and must include the whole abdominal field up to the diaphragm. Survivors into adult life, while not many, are not so rare that determined efforts of cure should not be made. Subsequent distant metastases, even including pulmonary spread, are worth further attempts at cure by radiation, owing to the well-marked radiosensitivity, but survivors are few.

Carcinoma of the ureter, though uncommon, should also receive post-operative therapy as the histology of these neoplasms indicates moderate responsiveness to irradiation.

Carcinoma of the bladder is a field which in recent years has been exploited with great success by the radiotherapist using interesting new techniques. The degree of improvement in cure rate, and the very satisfactory functional results, appears to be leading to the displacement of partial cystectomy as the routine treatment. Small carcinomas of the bladder, in any site, are best dealt with by open implantation methods using seeds, either of radioactive gold or containing radon. The carcinoma is exposed by cystotomy and after prior removal of exuberant growth with the diathermy loop, the seeds are inserted permanently, and the cystostomy is closed.

The indications for the use of this method are solitary lesions not exceeding 6 cm. in diameter, and not of a deeply infiltrating character. These indications should be most rigorously adhered to, since if success is not obtained the use of other methods suited to more extensive growth will be prevented. During the radiation reaction period, there may be frequency and pain on micturition, but this is usually surprisingly slight, though in the first few days retention due to blood clot formation should be watched for. The subsequent bladder function is very good and is often normal. The small growth at the fundus may be considered an exception to this policy, since the surgical results are satisfactory and a radon seed implant is technically difficult.

For the more extensive or deeply infiltrating lesion, X-ray therapy is employed. The course is prolonged and the attendant dysuria in the reacting period is often severe. Ultimate bladder function is variable, though some degree of frequency is usual, due to limitation of bladder capacity by scarring, and a degree of general contraction caused by the radiation. Persisting pain on micturition is usually a sign of residual growth. When

the neoplasm has spread outside the bladder, or pelvic lymph nodes are invaded, then X-ray therapy can only provide palliation. Pain, frequency and hæmaturia can be relieved by quite moderate dosage. In such cases, if total cystectomy and lymphadenectomy be possible this course should be adopted and post-operative radiotherapy used.

When the whole of the bladder surface is involved in multiple superficial papillomas, a new form of treatment has been devised consisting in the insertion of an inflatable rubber bag which is filled with a solution of a radioactive isotope. Beta ray emitters, such as phosphorus (32 P) or Strontium (90 Sr) are used, and the bladder mucosa is irradiated without affecting the deeper tissues. If a solution of an isotope emitting both beta and gamma rays of suitable energy be employed then deeper layers of tissue can be treated. By the use of a centrally placed radium or 60 cobalt source in the rubber bag, the whole thickness of the bladder wall can be dealt with, but the danger of contracted bladder subsequently is very high. In the female the inflatable bag is inserted through the urethra and in the male through a perineal urethrotomy. During the period of any radiation reaction in the bladder, infection should be kept to a minimum with suitable sulphonamides, and alkaline diuretics should be freely used.

Carcinoma of the penis is more certainly cured by surgery than by radiation, and this should be advised, especially in the advanced case. If the patient cannot be persuaded to accept surgery, then a radium mould or telecurietherapy for the small lesion is a practicable alternative. If the corpora are invaded radiation cure is remote. The reaction to radiotherapy is much more tolerable than might be supposed, and stricture formation is rare unless the urethra has been involved. Inguinal metastases should be dealt with by block dissection, if possible, as radiation only provides short lived palliation for secondary squamous carcinoma in groin glands.

Seminoma of the testis is perhaps the most radiosensitive of all tumours, and the treatment to be advised is orchidectomy followed by X-ray therapy, whether abdominal metastases are present or not. The cure rate when no abdominal glands are detectable is of the order of 80 per cent, compared to some 25 per cent with surgery alone. If abdominal spread is present the proportion of cures is still nearly 50 per cent. Delay after orchidectomy to see whether metastases become evident therefore nearly halves the patient's chance of survival. Even distant spread to lungs or mediastinum should not contraindicate the use of radiation, owing to the very high sensitivity.

Teratoma of the testis, on the other hand, is of very variable sensitivity depending upon the nature of the malignant constituent, but is mostly of a resistant character. Those patients who survive following orchidectomy and irradiation largely do so because metastases have not occurred before the operation, since X-ray therapy is rarely successful when palpable retroperitoneal spread is present. Nevertheless it is advisable to give post-operative radiotherapy in teratoma as well as seminoma, and it is an integral part of the curative treatment policy. During the radiation treatment of the abdomen, the scrotum, and unaffected testis are shielded from the rays if there has been no attachment of the neoplasm to the scrotal skin. This is advisable in spite of a rather greater liability than normal of the second testis to undergo malignant change, as thereby sexual potency is retained. Some scattered radiation always reaches the shielded testis and in most cases this diminishes fertility greatly

Carcinoma of the prostate is not now treated by radiation, and it is in any case of a resistant character. When œstrogen therapy has ceased to control the tumour, palliative

radiotherapy may provide moderate symptomatic relief, and is certainly worthwhile trying for painful bone secondaries.

Carcinoma of the scrotum should be excised.

Carcinoma of the Alimentary Tract

Carcinomas in the pharynx and œsophagus have already been dealt with, but carcinomas of the stomach, small intestine, colon, liver, gall bladder, and pancreas, all present problems in which radiotherapy has no part to play. The rare reticulo- or lymphosarcomas which may be found should receive X-ray therapy treatment by wide field methods, preferably after as complete a removal surgically as is possible.

Carcinoma of the rectum has been treated in the past by various radiation methods, always with noticeable lack of success. In cases of inoperability or of local recurrence after excision, some degree of palliation can be obtained, especially with super-voltage radiation.

Intracranial Tumours

Gliomas, with the exception of medulloblastoma, are a group of neoplasms which have a low degree of sensitivity to radiation, but as with other malignant tumours sensitivity is greater in the more anaplastic varieties. For astrocytomas, the generally accepted treatment policy is to rely upon excision in the more differentiated tumours, using radiotherapy for those that are inoperable or have been incompletely removed. Post-operative radiotherapy should be given in the undifferentiated group whether apparently completely removed or not. Oligodendrogliomas, ependymomas, and choroidal papillomas are treated on the same pattern as astrocytomas but are said to produce rather better results.

For medulloblastomas the policy is different, since it is unnecessary, or as some aver, inadvisable, to attempt operative removal. A decompression and biopsy should always be done, however, and irradiation should commence without delay. The whole of the cerebral ventricular system and the subarachnoid spaces, including the spinal canal must be irradiated as well as the tumour, owing to the frequent spread of metastases through the cerebro-spinal fluid. The treatment course is prolonged, technically difficult, and often stormy, but the results are encouraging. Survivors after 5 years may be as high as 40 per cent. When occurring in an adult the prognosis is less favourable. Recurrences may be retreated with symptomatic relief for short periods.

Meningiomas are, as a class, not sensitive to radiation and therapy is only employed if they are too vascular for surgical removal, or are so situated as to make removal hazardous, notably at the base of the brain. The treatment, when effective, is probably due to shrinkage of the highly vascular varieties.

For primary cerebral neoplasms, it is essential to use all ancillary aids to the establishing of the precise site and extent of the tumour, even if certainly inoperable, or the radiotherapist will be working at a grave disadvantage. It is advisable that craniotomy should be done in as many cases as possible, to site the neoplasm accurately, to obtain a biopsy, and to provide decompression. If any brain swelling occurs subsequent to the institution of radiotherapy, there is then little danger from cerebral compression. The modern tendency is towards moderate rather than high radiation dosage, and the results do not seem to have worsened as a consequence. With high dosage, radiation degeneration of brain substance can take place, often some years after treatment, and it is usually impossible to distinguish this from recurrence. It is probable that cure of a cerebral tumour

by radiation cannot be obtained without some normal tissue degeneration, though only the more extensive degrees become clinically apparent.

Pituitary adenomas are all treatable by X-ray therapy but little beyond regression of symptoms may be expected, though sometimes this is prolonged for years. The eosinophil variety respond most favourably, and the visual field defects lessen, though headache is not so constantly relieved. Comparatively low dosage, which can be repeated, is used. The chromophobe tumours are less responsive and high dosage must be used, but long term good results are not uncommon. Basophil adenomas rarely respond to irradiation *though one or two spectacular results have been reported. Pituitary irradiation in Cushing's* Syndrome is similarly disappointing.

Spinal tumours follow the general pattern outlined for cerebral tumours. The not uncommon lympho-reticular sarcomas, or allied reticuloses, which occur extradurally but often penetrate and spread widely within the theca, are very radiosensitive and pressure symptoms can be dramatically relieved by X-ray therapy. If localized, a permanent cure may be obtained, but the spinal tumour is usually a manifestation of more generalized disease. Spinal and cerebral hæmangiomas which cannot be removed surgically, may also be responsive to radiation, especially in the variety showing vessels of only small calibre. Chordomas may be treated with palliative response, but unless the main tumour has been previously excised, such response is not lasting. Neurofibromas and neurofibrosarcomas of cauda equina and nerve roots are not radiosensitive though some palliation of symptoms may be expected.

Neuroblastomas usually present as secondary deposits, often in lymph nodes and show a moderately radiosensitive response. The large retroperitoneal neuroblastomas encountered in infancy should be treated by radiation, and if distant metastases are absent a few apparent cures have been obtained.

Bone and Soft Tissue Tumours

Osteogenic sarcomas are highly radio-resistant. Since the results of surgical treatment are so disappointing, some combination of radiotherapy and surgery is worth attempting, and a few survivals are reported following X-ray therapy to higher than the accepted tolerance dosage, with subsequent amputation if necrosis supervenes. Chondrosarcomas are uniformly quite insensitive to radiation.

Osteoclastomas respond to repeated moderate dosage radiation courses by healing with reossification In the early post-radiation period a more extensive loss of bone substance is usually visible on the radiographs, but this must not be interpreted as extension of the disease. A biopsy is advisable prior to radiation therapy, though it is not possible to exclude malignancy entirely thereby, owing to the difficulty of obtaining fully representative samples. A lack of success with radiation in adequate dose is believed by some to imply wrong diagnosis, and that the lesion is malignant.

Hæmangiomas of bone respond well to moderate dose radiation with early relief of symptoms. The radiological changes of consolidation and reossification are usually long delayed.

Simple bone cysts do not as a rule show an adequate radiation response, and surgical measures are indicated if practicable.

Reticulosarcomas of bone are apparently curable by radiation, provided that all the diseased tissue is treated and it is therefore advisable to include the whole bone in the

treatment zone. It seems probable that many examples of Ewing's Tumour fall into this group, and that others are secondary tumours, often neuroblastomas. Whether there is a specific Ewing's Tumour remains in doubt.

Adamantinomas are certainly responsive to radiation and teleradium methods appear to give the best results. Many cases recur and demand further attempts at cure, either by surgery or more radiation, and opinion appears to be hardening that a planned initial approach with combined pre-operative radiation and surgery is advisable.

Myelomas reossify and pain is relieved without needing high dose, and the myelomatous masses occasionally occurring in soft tissue also respond. The fully developed myelomatosis may be helped by palliative exposures for pain relief.

Paget's disease is not affected by radiation. On occasions pain in a limb may be relieved but usually only for a short time

Synoviomas are radiosensitive, and the use of radiation, either as the primary treatment, or post-operatively, is to be recommended.

Fibrosarcomas vary in their immediate response to radiation though usually a very high dosage is needed to affect them. The very great majority recur, and radical surgery is in consequence the treatment of choice. Post-operative irradiation is not called for and may be held in reserve to palliate recurrence. Radiotherapy has no part to play in the treatment of sarcomas of muscle.

The sarcomas of lymphoreticular tissue should be treated by radiation in whatever site they occur. If localized, a cure rate of approaching 50 per cent can be obtained by treating the neoplasm with wide margins and including in continuity the whole of the relevant lymph node group. More widespread deposits may be treated palliatively, and many years survival may be obtained in some cases of generalized disease.

CHAPTER X

THE ADRENAL GLANDS

RICHARD B. WELBOURN

ANATOMY

THERE are two adrenal (suprarenal) glands, one lying at the upper pole of each kidney between the two layers of the renal fascia. They are relatively inaccessible, being placed deeply in the retro-peritoneal tissues and related posteriorly to the crura of the diaphragm. The right adrenal is pyramidal in shape, sits like a cap on the upper pole of the kidney and is closely related to the inferior vena cava medially and to the liver anteriorly. The left gland is semilunar in shape, extends some distance down the medial side of the kidney and is related medially to the aorta and anteriorly to the pancreas and lesser sac of the peritoneum.

The adrenals are relatively large in infancy. In the adult each gland weighs about 5–6 gm. Their colour is orange and enables them to be distinguished easily from the adjacent structures and fat.

The small arteries which supply the adrenals are derived from the aorta and from the inferior phrenic and renal arteries and break up into many small arterioles before entering the glands. The adrenal veins are larger and there is usually one main vessel on each side. That on the right is short and enters the vena cava directly, while that on the left joins the renal vein either directly or after forming a common trunk with the inferior phrenic. Variations, such as duplication of the veins, are common on both sides.

The adrenals consist of two parts, a larger, outer cortex and a smaller, inner medulla, which are embryologically and functionally distinct.

ADRENAL CORTEX

The cortex has three histologically distinct zones, named (from without inwards): (1) the zona glomerulosa, (2) the zona fasciculata and (3) the zona reticularis. A fourth (inner) zone, the "fœtal cortex," disappears within a few weeks of birth. Small accessory collections of adrenal cortical cells are often present near the main glands, elsewhere in the retro-peritoneal tissues, in the broad ligaments of the uterus or in the spermatic cords.

PHYSIOLOGY

The adrenal cortex is essential to life. It is an organ of internal secretion and produces three main types of highly active steroids, which are listed in order of importance.

(1) **Glucocorticoids**, the most active of which is hydrocortisone (compound F), are probably formed in the zona fasciculata. They raise the blood sugar, promote the storage of carbohydrate and fat, bring about the breakdown of protein and inhibit inflammatory and allergic reactions. They also have weak "electrocorticoid" and androgenic effects (see below) and various other less important actions, including destruction of the eosinophil leucocytes. Cortisone (compound E) and its analogues have similar actions.

The secretion of glucocorticoids is controlled mainly by corticotrophin (ACTH), which is produced by the anterior lobe of the pituitary in response to various stimuli, including the stress of trauma or of a surgical operation. The secretion of corticotrophin is also regulated by the concentration of hydrocortisone in the blood, so that a reciprocal control exists between the pituitary and the adrenal. Thus, if there is an adequate or excessive amount of hydrocortisone in the body the production of corticotrophin is inhibited, while if there is insufficient hydrocortisone to meet the body's requirements the secretion of corticotrophin is stimulated and more adrenal corticoids are produced. Cortisone and its analogues similarly inhibit the formation of corticotrophin.

(2) Electrocorticoids, the most active of which is aldosterone, are probably formed in the zona glomerulosa. They promote the retention of sodium, chloride and water and the excretion of potassium. Their secretion is regulated mainly by the electrolyte and water content of the body and slightly by corticotrophin. Deoxycortone (DCA) is a synthetic steroid with a similar, but much weaker, action.

(3) Sex hormones, which are of three main types, namely androgens, oestrogens and progesterones, are probably formed in the zona reticularis. Their physiological effects are uncertain, but they may assist in the actions of the hormones produced by the gonads, and under certain conditions can influence profoundly the primary and secondary sex characters. The androgens also promote the synthesis of protein and retention of nitrogen, may exert a weak "electrocorticoid" effect and can support the growth of prostatic carcinoma. The œstrogens can sustain the growth of mammary carcinoma. A progesterone (17-hydroxyprogesterone), which has androgenic properties, is thought to be a pre-cursor of hydrocortisone (17-hydroxycorticosterone). The secretion of sex hormones by the adrenals is largely under the control of corticotrophin.

The adrenal steroids are metabolized to a large extent in the tissues and then excreted in the urine either in their original form or as derivatives. Their measurement in the urine provides a partial index of their secretion and is used extensively in the investigation of adrenal disorders.

PATHOLOGY

Lesions of the adrenal cortex frequently cause disturbance of endocrine function. Various clinical syndromes may result, depending on whether the secretion is increased or diminished and, when it is increased, which hormones predominate. The lesions and syndromes may be classified as follows:

A. With Disturbance of Endocrine Function

1. Increased Secretion

Lesions:

(i) Hyperplasia.
(ii) Adenoma.
(iii) Carcinoma.

Syndromes:

Excess of glucocorticoids causes Cushing's syndrome.
Excess of electrocorticoids causes hyperaldosteronism.
Excess of androgens causes virilism.
Excess of œstrogens causes feminization.

2. Decreased Secretion

Lesions:

(i) Atrophy.
(ii) Destruction by hæmorrhage, infarct, tuberculosis, metastatic carcinoma, etc.
(iii) Surgical removal.

Syndromes:

Chronic deficiency causes Addison's disease.
Acute deficiency causes acute adrenal failure (adrenal crisis).

B. Without Disturbance of Function

Lesions:

(i) Adenoma.
(ii) Carcinoma.
(iii) Rare tumours, cysts, etc.

Hyperplasia is usually bilateral. The number of cells is increased, the cortex as a whole is enlarged and there is increased production of hormones. Hyperplasia may be caused by the prolonged therapeutic administration of corticotrophin and may also be found in Cushing's syndrome, adrenal virilism and hyperaldosteronism. It is recognized by the size of the glands, which may be greatly enlarged and, in infants, may be as large as the kidneys. In Cushing's syndrome routine staining reveals no special histological features. In adrenal virilism there is hyperplasia of the zona reticularis and reduction or absence of the zona fasciculata, and the fuchsinophil staining reaction of Vines is usually positive. The pathogenesis of these two types of hyperplasia will be discussed later.

Atrophy is also usually bilateral. The number of cells is decreased, the gland is diminished in size and there is reduced function. Atrophy is found in the following conditions:

(1) Hypopituitarism (Simmond's disease) and hypophysectomy, which cause a failure of corticotrophin production.

(2) Prolonged therapeutic administration of cortisone or its analogues, which inhibit the production of corticotrophin.

(3) Adreno-cortical tumours (adenoma and carcinoma) which form hydrocortisone or related substances. These inhibit the pituitary with the result that the adrenal cortex (on the same and on the opposite side), which is not involved by tumour, undergoes atrophy. Non-functioning tumours and those which secrete mainly androgens do not cause atrophy.

The atrophied glands may be half the size of the normal adrenals or even smaller. There are no special histological features.

Tumours

Cortical nodules, 2–3 mm. in diameter, are very common in normal glands. Benign adenomata are not uncommon and are usually found at autopsy without having given rise to symptoms during life. They are circumscribed, roughly circular, orange in colour, usually not more than 2–3 cm. in diameter, and rarely multiple. Their structure is similar to that of the normal adrenal cortex. Carcinoma is rare, but may occur at any age and is commonest in women between the ages of 25 and 45. The size of these tumours varies enormously, the largest weighing between 1 and 2 kgm. Their colour is similar to that of

the normal cortex. Some are well differentiated and circumscribed and are barely distinguishable from adenomata, while others are anaplastic, pleomorphic and invasive, and metastasize early to the lungs, the liver and elsewhere. Hæmorrhage and necrosis are common in the larger tumours.

Both adenomata and carcinomata (and their metastases) may or may not be functionally active, and their activity bears no relation to their size. They may cause any of



FIG 184 X-ray following intravenous pyelography and presacral insufflation of gas, showing normal left supra-renal and a tumour of the right gland The tumour was not palpable and was not demonstrable by simpler methods. (Professor C A Wells' case.)

the syndromes of hyperadrenocorticism, depending on the hormones which they secrete. The secretions of adenomata are usually partly under corticotrophin control, but those of carcinomata are autonomous. In Cushing's syndrome the non-tumorous cortical tissue undergoes atrophy. In cases of virilism the tumour cells usually give a positive Vines reaction.

INVESTIGATION OF ADRENOCORTICAL DISORDERS

(1) Radiology

Radiology, though usually disappointing, is sometimes helpful in detecting the presence of adrenal tumours or hyperplasia. Large tumours may be visible in straight radiographs of the abdomen. A greater number can be found by intravenous pyelography,

2. Decreased Secretion

Lesions:

(i) Atrophy.
(ii) Destruction by hæmorrhage, infarct, tuberculosis, metastatic carcinoma, etc.
(iii) Surgical removal.

Syndromes:

Chronic deficiency causes Addison's disease.
Acute deficiency causes acute adrenal failure (adrenal crisis).

B. Without Disturbance of Function

Lesions:

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(3) Adreno-cortical tumours (adenoma and carcinoma) which form hydrocortisone or related substances. These inhibit the pituitary with the result that the adrenal cortex (on the same and on the opposite side), which is not involved by tumour, undergoes atrophy. Non-functioning tumours and those which secrete mainly androgens do not cause atrophy.

The atrophied glands may be half the size of the normal adrenals or even smaller. *There are no special histological features.*

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one-third is produced by the testes. The total urinary excretion during a 24-hour period is determined chemically. Two fractions of the 17-ketosteroids can be distinguished, and their relative proportions may be disturbed in disease states. The "α-fraction" is formed both by the adrenals and by the testes, while the "β-fraction" is produced by the adrenals only.

Low values are found following atrophy or destruction of the adrenal cortices, after adrenalectomy and in some other apparently unrelated conditions. High values are found after corticotrophin therapy, in adrenal virilism, especially when it is caused by a malignant tumour, and in some cases of Cushing's syndrome.

A useful test for distinguishing between benign and malignant lesions in cases of virilism, and possibly in some cases of Cushing's syndrome, is provided by the response of the 17-ketosteroid excretion to the administration of glucocorticoids. In hyperplasia and often in adenoma these hormones cause a fall in 17-ketosteroid excretion by inhibiting the production of corticotrophin on which the hyper-activity of the adrenal cortex depends. In cases of carcinoma no fall is produced since the neoplastic cells are not under corticotrophin control.

(ii) "17-KETOGENIC STEROID" EXCRETION

The excretion of "17-ketogenic steroids" in a 24-hour sample of urine provides a useful index of glucocorticoid excretion. The 17-ketosteroids are measured both before and after the urine has been treated chemically to convert the glucocorticoids into 17-ketosteroids. The difference between the two readings represents the 17-ketogenic steroids.

Low values are found following atrophy or destruction of the adrenal cortices, after adrenalectomy and in cases of cortical hyperplasia associated with adrenal virilism. High values are found in many cases of Cushing's syndrome.

(iii) "17-HYDROXYCORTICOID" EXCRETION

The "17-hydroxycorticoids" are hydrocortisone and its analogues and represent the main glucocorticoid excretion of the adrenal cortex. Like the 17-ketosteroids their excretion in a 24-hour specimen of urine is determined chemically. Alterations in their excretion in different states are very similar to those of the 17-ketogenic steroids. The test is highly specific, but of limited value.

(3) Eosinophil Count (Thorn Test)

Estimation of the number of circulating eosinophil leucocytes provides another partial index of adrenal function. Glucocorticoid excess depresses the eosinophil count, while deficiency tends to raise it. The eosinophils, however, are influenced by many factors and less reliance should be placed on the absolute count than on the depression of cells following the administration of corticotrophin. A suitable method of performing the test is to combine it with the stimulation test described in Table I. A count is performed in the fasting state immediately before the first injection of corticotrophin and another is made seven hours later. If adrenal cortical function is normal or increased the count should fall at least 50 per cent. If the decrease in eosinophils is less than 30 per cent cortical function is probably impaired. Intermediate values are equivocal.

which may show distortion or displacement of a kidney. Probably the best method of demonstrating the adrenals, however, is that of tomography after the glands have been outlined by carbon dioxide. (Other gases may cause death from embolism.) About 1500 ml. are injected through a polythene tube behind the rectum and pass up between the layers of the renal fascia, outlining the kidneys and adrenals. Gross hyperplasia and many tumours can be recognized by this method, but there is a large margin of error. Aortography may be helpful, but its possibilities have not been fully explored.

(2) Biochemical Tests

The following tests of cortical steroid excretion give the most helpful information at the present time, but new ones are being developed constantly. Isolated estimations are of limited value and whenever possible the effects of stimulation or inhibition of the adrenal cortex should be determined. Typical results in various conditions are given in Table I.

TABLE I

URINARY EXCRETION OF ADRENAL CORTICAL STEROIDS

Representative levels in normal and pathological states
(All values in mg. per 24 hrs.)

	17-ketosteroids		17-ketogenic steroids	
	Basal	Corticotrophin Stimulation (1)	Basal	Corticotrophin Stimulation (1)
Normal:				
Men . .	10–20	15–40	10–20	40–70
Women .	5–15		5–15	
Children (0–2 years) .	1		2	
Cushing's Syndrome:				
Hyperplasia or hyperfunction.	10–40	15–60	10–40	60–150
Carcinoma . . .	10–300	No rise	50–100	No rise
Addison's Disease . .	0–5	No rise	0–5	No rise
Hypopituitarism	0–5	5–15	0–5	5–15
		Hydrocortisone Suppression (2)		
Adreno-genital Syndrome:				
Hyperplasia	10–100	5–20	0–20	
Children (0–2 years)	2–5	0.5–1	0–2	
Carcinoma .	50–500	No fall	5–80	

(1) Urine is collected for 6 successive 24-hour periods. The first 2 days give the basal secretion. From the 3rd to the 6th day 20 clinical units of corticotrophin-gel are given intramuscularly twice daily. The last 2 days give the "stimulated" secretion.

(2) Urine is collected for 2 successive 24-hour periods. The first day gives the basal secretion. During the whole of the 2nd day 50 mg. of hydrocortisone in 250 ml. of a solution of 5 per cent glucose and 1 per cent alcohol is infused intravenously at a constant rate. The second day gives the "suppressed" secretion.

(i) "17-KETOSTEROID" EXCRETION

The "17-ketosteroids" are largely, though not entirely, derived from androgenic steroids. In the female their only source is the adrenal cortex, while in the male about

one-third is produced by the testes. The total urinary excretion during a 24-hour period is determined chemically. Two fractions of the 17-ketosteroids can be distinguished, and their relative proportions may be disturbed in disease states. The "α-fraction" is formed both by the adrenals and by the testes, while the "β-fraction" is produced by the adrenals only.

Low values are found following atrophy or destruction of the adrenal cortices, after adrenalectomy and in some other apparently unrelated conditions. High values are found after corticotrophin therapy, in adrenal virilism, especially when it is caused by a malignant tumour, and in some cases of Cushing's syndrome.

A useful test for distinguishing between benign and malignant lesions in cases of virilism, and possibly in some cases of Cushing's syndrome, is provided by the response of the 17-ketosteroid excretion to the administration of glucocorticoids. In hyperplasia and often in adenoma these hormones cause a fall in 17-ketosteroid excretion by inhibiting the production of corticotrophin on which the hyper-activity of the adrenal cortex depends. In cases of carcinoma no fall is produced since the neoplastic cells are not under corticotrophin control.

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(iii) "17-HYDROXYCORTICOID" EXCRETION

The "17-hydroxycorticoids" are hydrocortisone and its analogues and represent the main glucocorticoid excretion of the adrenal cortex. Like the 17-ketosteroids their excretion in a 24-hour specimen of urine is determined chemically. Alterations in their excretion in different states are very similar to those of the 17-ketogenic steroids. The test is highly specific, but of limited value.

(3) Eosinophil Count (Thorn Test)

Estimation of the number of circulating eosinophil leucocytes provides another partial index of adrenal function. Glucocorticoid excess depresses the eosinophil count, while deficiency tends to raise it. The eosinophils, however, are influenced by many factors and less reliance should be placed on the absolute count than on the depression of cells following the administration of corticotrophin. A suitable method of performing the test is to combine it with the stimulation test described in Table I. A count is performed in the fasting state immediately before the first injection of corticotrophin and another is made seven hours later. If adrenal cortical function is normal or increased the count should fall at least 50 per cent. If the decrease in eosinophils is less than 30 per cent cortical function is probably impaired. Intermediate values are equivocal.

(4) Surgical Exploration

Full investigation may fail to reveal or exclude the presence of a tumour. Surgical exploration of one or both glands is then necessary and should be undertaken without hesitation.

CUSHING'S SYNDROME

Cushing's syndrome is a rather uncommon condition, which may be caused by the following lesions:

(1) **Adrenocortical hyperplasia,**

(2) **Adrenocortical hyperfunction** without hyperplasia.

These are the two commonest findings in adults, and hyperplasia is always present in the rare congenital cases. Their cause is uncertain, but there may be:



FIG. 185 Cushing's syndrome in a girl of 18 Note the moon face, florid complexion, trunk obesity, buffalo hump and purple striæ.

(i) Reduced sensitivity of the anterior pituitary to inhibition by circulating hydrocortisone, resulting in excessive secretion of corticotrophin; or

(ii) Excessive response of the adrenal cortex to normal amounts of corticotrophin.

(3) **Adrenocortical Tumour** (adenoma or carcinoma). This is the commonest cause in children, but is much less common in adults.

(4) **Basophil adenoma** of the anterior pituitary is rare but, when present, the terms "Cushing's disease" or "pituitary basophilism" are applicable. The adenomata presumably secrete corticotrophin, but are usually too small to cause enlargement of the sella turcica or pressure symptoms. Hyalinized basophil cells ("Crooke's cells"), which are found constantly in the pituitary in Cushing's syndrome, are functionally inactive and are probably the result, rather than the cause, of hyperadrenocorticism.

(5) **Hypothalamic and Ovarian Lesions.** These are extremely rare. A few cases have also been reported in which the syndrome was associated with liver disease or with carcinoma of the bronchus, thymus or pancreas.

The syndrome may be reproduced by the prolonged therapeutic

administration of corticotrophin or cortisone and it is clear that excessive adrenocortical secretions are responsible for all the clinical and metabolic features. The gluco-corticoid (or pure "Cushing's") features predominate but some signs of virilism are frequently present and, when marked, are usually the result of excess androgen secretion.





Figs 186 and 187 The same patient before and again six months after sub-total adrenalectomy.

Clinical Features

The syndrome may develop at any age and is very rarely congenital. The average age of onset is about 30 and women are affected much more commonly than men. An adrenocortical tumour is very rarely palpable.

I. Effects of Glucocorticoid Excess. (1) Deposition of fat causes a characteristic type of *obesity* which affects the face and trunk, but spares the limbs. The face assumes a round "full-moon" shape and there are usually subcutaneous pads of fat in the supra-clavicular and cervico-dorsal regions, the latter causing the typical "buffalo hump." There is usually an increase in body weight.

(2) Protein breakdown affects mainly the muscles, the skin and the bone matrix and causes a negative nitrogen balance. *Muscle wasting* is obvious in the limbs and *lethargy and weakness* are frequent complaints. Atrophy of the skin causes a *florid complexion* and *purple striæ* of the trunk and proximal parts of the limbs. Atrophy of the bone matrix gives rise to *osteoporosis* and *backache*, and *spinal deformities* and *pathological fractures*, especially of the ribs and vertebræ, are common. Hypercalciuria follows and

urinary calculi sometimes develop. Atrophy of the capillary walls causes a liability to *purpura* and *bruising*.

(3) Disordered carbohydrate metabolism sometimes causes *diabetes mellitus.*

(4) Inhibition of inflammatory reactions renders the patients very liable to *severe infections* of the respiratory tract and elsewhere.

(5) Disturbances of electrolyte metabolism include retention of sodium and water, and excretion of potassium. Water retention sometimes causes *œdema* and is probably the main cause of the *arterial hypertension,* which is usually present, often severe and liable to all the complications of essential hypertension. Excessive potassium excretion often causes *hypokalæmic alkalosis* and there may be *latent tetany.*

(6) Changes in the blood include a tendency to *polycythæmia,* which contributes to the patient's high colour, and alterations in the leucocytes.

(7) *Hyperchlorhydria* is common.

(8) *Mental changes,* ranging from lability of mood to frank psychosis, are common.

II. Effects of Androgen Excess. Virilism is less marked than it is in the adreno-genital syndrome, but amenorrhœa is usual, hirsutism and acne are common and the clitoris sometimes enlarges slightly. Impotence is usual in men, but its cause is not clear.

Prognosis

Although there may be spontaneous partial remissions, the prognosis of the untreated disease is bad. Half the patients die within 5 years of its onset from the effects of hypertension, diabetes and infections.

Investigations

There are two main questions to be answered: first, "is this a case of Cushing's syndrome?" and secondly, "what is the nature and site of the underlying lesion?"

(1) Urinary steroids. The 17-ketosteroid excretion is raised in about half the patients, especially in those with virilism. The levels, however, are rarely high enough to show a striking fall after the administration of glucocorticoid. Very high levels almost always indicate a carcinoma. The 17-ketogenic steroids and the 17-hydroxycorticoids are often, but not always, raised, especially after stimulation with corticotrophin. The rise is greatest with hyperplasia and less marked with adenoma, while carcinomata usually give high resting values which are unaffected by corticotrophin.

(2) Serum electrolytes. Hypokalæmia and alkalæmia are common. The serum chloride level is variable.

(3) Hæmatology. Polycythæmia, neutrophil granulocytosis, eosinopenia, and lymphopenia are common

(4) Carbohydrate metabolism. Glycosuria and a diabetic type of glucose tolerance curve are quite common. The hyperglycæmia is insulin-resistant.

(5) Electro-cardiogram Left ventricular hypertrophy or strain, coronary artery disease and hypokalæmia may cause characteristic changes.

(6) Radiology. Generalized osteoporosis is usual. In the spine this may cause "cod-fish" vertebræ, kyphosis, scoliosis and pathological compression fractures. Healed fractures are often seen in the ribs. The heart and aorta may show the effects of hyper-tension. The sella turcica is almost always normal in size, although the osteoporosis

may make it appear large. X-rays of the adrenals may reveal hyperplasia or a tumour.

(7) Pelvic examination must be undertaken to exclude an ovarian tumour.

Differential Diagnosis

Various conditions may be confused with Cushing's syndrome. Simple obesity does not spare the limbs. Essential hypertension is often associated with obesity, but not usually with other features of the disease. In the adreno-genital syndrome the muscles are often well developed and other signs of virilism are prominent.



FIG 188 X-ray of spine in Cushing's syndrome Note the osteoporosis, "codfish" vertebræ and pathological compression fracture

Treatment

The grave prognosis in Cushing's syndrome makes early treatment essential. The hypokalæmic alkalosis should be corrected by potassium chloride (2 gm. three times a day, by mouth) and infections must be controlled by antibiotics. The other features, however, are rarely affected by medical measures and irradiation of the pituitary is only sometimes effective. Surgery at present offers the best hope of cure and it should be advised unless the patient is too ill. In the very rare cases in which a basophil adenoma

can be demonstrated hypophysectomy is indicated. Removal or irradiation of the pituitary is less satisfactory than adrenalectomy in other cases. If an ovarian tumour is palpable it should be removed and examined before further surgery is undertaken.

In most cases, however, adrenalectomy is the treatment of choice. In the absence of a tumour at least nine-tenths of the hyperplastic or hyperfunctioning adrenal tissue is excised. Less extensive resections are uncertain in their effects and the only point at issue is whether the adrenalectomy should be total or sub-total. Sub-total removal produces a clinical remission in all cases and many of the patients require no cortisone replacement therapy after the first few months. A small (and as yet unknown) proportion, however, relapse later and require a further operation for removal of the remaining portion of gland which may have increased greatly in size and in functional capacity. The effects of total adrenalectomy are probably more lasting, but permanent cortisone replacement is necessary and life is relatively precarious. Unless future experience shows that relapses are common, removal of nine-tenths of one gland and all of the other would seem to be the procedure of choice.

If a tumour can be located before operation the gland on that side is explored and the tumour removed. Any adrenal tissue which is not involved is also resected (at least sub-totally) since the tumour itself may not be functionally active. The other gland need only be explored if a remission does not ensue. It is worthwhile attempting to remove a carcinoma, even in the presence of metastases, since a temporary remission may follow.

If no tumour has been located the *left* gland is explored first since it is the more accessible and the easier to resect sub-totally. When it has been exposed three courses are possible:

(1) If a tumour is found, it is removed.

(2) If the gland is atrophic it is probable (but not certain) that there is a tumour on the opposite side. A biopsy is taken and the other gland explored later.

(3) If the gland is normal or hyperplastic it is resected sub-totally and the whole of the other gland is removed later.

Results of Surgical Therapy

The immediate post-operative period may cause anxiety, but with proper care the operative mortality is low. Within a few weeks the appearance starts to return towards normal and the process is usually complete within about six months. The skin of the face, and sometimes of the body, undergoes a fine scaly desquamation, which causes itching. Weight is lost, strength and energy are regained and a normal bodily configuration returns. Signs of virilism diminish, but rarely disappear completely. The hair becomes lighter and softer and sexual function is restored. (Sterility persists after destruction or removal of the pituitary.) The bones become re-calcified rather slowly and back-ache may persist longer than the other symptoms. Spinal deformities become stabilized. Brown pigmentation of the Addisonian type usually develops temporarily in the operation scars and sometimes elsewhere. The blood pressure (both systolic and diastolic) falls significantly in all, but returns to normal in only a few. Irreversible cardiovascular changes which were present before operation continue to endanger life, and the ultimate prognosis following surgery is not yet known. The early results, however, indicate that operation is well worthwhile.

THE ADRENO-GENITAL SYNDROME

The adreno-genital syndrome is a rare condition, which may be caused by a tumour (adenoma or carcinoma) or by hyperplasia of the adrenal cortex. The essential lesion in hyperplasia is probably biochemical and consists of a failure to synthesize hydrocortisone, excessive amounts of its pre-cursor, 17-hydroxyprogesterone, being produced instead. This substance is androgenic and, unlike hydrocortisone, does not inhibit the production of corticotrophin by the pituitary. Consequently there is hypersecretion of corticotrophin, hyperplasia of the adrenal cortex (affecting mainly the zona reticularis), excessive production of 17-hydroxyprogesterone and other androgens and deficiency of glucocorticoids. There may also be deficiency of electrocorticoid, although the reason for this is not clear.

The adrenal androgens, which are formed in neoplastic or hyperplastic glands, are responsible for the main clinical features of the syndrome. In some patients, especially those with tumours, there is an excess of glucocorticoids and these may cause some features of Cushing's syndrome. Forms intermediate between the two syndromes are not uncommon.

Clinical Features

The clinical picture varies with the age and sex of the patient, and the following table shows the main varieties:

Period	Lesion	Male Syndrome	Female Syndrome
Infancy (Congenital)	Hyperplasia	Macro-genitosomia praecox "Infant Hercules"	Female pseudohermaphroditism
Childhood (Pre-pubertal)	Usually tumour		
Adult life (Post-pubertal).	Hyperplasia or tumour	Excessive virilism	Virilism

Post-pubertal virilism in the female is caused more commonly by hyperplasia than by tumour and varies greatly in severity. The onset is gradual with hyperplasia and more rapid with a tumour. A large tumour may be palpable. The androgens have three main effects: a direct virilizing action on the tissues, causing the development of male sex characters, an inhibiting effect on the pituitary, causing the regression of female sex characters and some non-specific actions. *The virilizing effects* are: hirsutism of a male type on the face, trunk and limbs, followed sometimes by baldness; growth of the larynx with deepening of the voice; muscular development with increased physical stamina; aggressiveness and increased libido; and hypertrophy of the clitoris, sometimes with frequent erections. *Regression of the female sex characters* is reflected in scanty periods or amenorrhœa, sterility, atrophy of the breasts, loss of subcutaneous fat and atrophy of the external genitalia (except the clitoris). The *non-specific actions* include a general anabolic effect, with nitrogen retention and increase of weight; greasiness and acne of the skin; and hypertension. The latter, which is an occasional feature of the syndrome, may be the result of fluid and salt retention. The *mental reactions* to these changes may cause serious maladjustment.

Post-pubertal virilism in the male causes excessive masculinization, which rarely attracts attention.

can be demonstrated hypophysectomy is indicated. Removal or irradiation of the pituitary is less satisfactory than adrenalectomy in other cases. If an ovarian tumour is palpable it should be removed and examined before further surgery is undertaken.

In most cases, however, adrenalectomy is the treatment of choice. In the absence of a tumour at least nine-tenths of the hyperplastic or hyperfunctioning adrenal tissue is excised. Less extensive resections are uncertain in their effects and the only point at issue is whether the adrenalectomy should be total or sub-total. Sub-total removal produces a clinical remission in all cases and many of the patients require no cortisone replacement therapy after the first few months. A small (and as yet unknown) proportion, however, relapse later and require a further operation for removal of the remaining portion of gland which may have increased greatly in size and in functional capacity. The effects of total adrenalectomy are probably more lasting, but permanent cortisone replacement is necessary and life is relatively precarious. Unless future experience shows that relapses are common, removal of nine-tenths of one gland and all of the other would seem to be the procedure of choice.

If a tumour can be located before operation the gland on that side is explored and the tumour removed. Any adrenal tissue which is not involved is also resected (at least sub-totally) since the tumour itself may not be functionally active. The other gland need only be explored if a remission does not ensue. It is worthwhile attempting to remove a carcinoma, even in the presence of metastases, since a temporary remission may follow.

If no tumour has been located the *left* gland is explored first since it is the more accessible and the easier to resect sub-totally. When it has been exposed three courses are possible:

(1) If a tumour is found, it is removed.

(2) If the gland is atrophic it is probable (but not certain) that there is a tumour on the opposite side. A biopsy is taken and the other gland explored later.

(3) If the gland is normal or hyperplastic it is resected sub-totally and the whole of the other gland is removed later.

Results of Surgical Therapy

The immediate post-operative period may cause anxiety, but with proper care the operative mortality is low. Within a few weeks the appearance starts to return towards normal and the process is usually complete within about six months. The skin of the face, and sometimes of the body, undergoes a fine scaly desquamation, which causes itching. Weight is lost, strength and energy are regained and a normal bodily configuration returns. Signs of virilism diminish, but rarely disappear completely. The hair becomes lighter and softer and sexual function is restored. (Sterility persists after destruction or removal of the pituitary.) The bones become re-calcified rather slowly and back-ache may persist longer than the other symptoms. Spinal deformities become stabilized. Brown pigmentation of the Addisonian type usually develops temporarily in the operation scars and sometimes elsewhere. The blood pressure (both systolic and diastolic) falls significantly in all, but returns to normal in only a few. Irreversible cardiovascular changes which were present before operation continue to endanger life, and the ultimate prognosis following surgery is not yet known. The early results, however, indicate that operation is well worthwhile.

and electrocorticoid insufficiency may cause salt loss, feeding difficulties, loss of weight, vomiting, dehydration and death.

As the child grows up signs of virilism appear, similar to those seen in the adult female, and there is primary amenorrhœa. In addition there are striking abnormalities of skeletal development. Body growth is unusually rapid at first and the ossification



FIG 190. Enlargement of clitoris in the adreno-genital syndrome (female pseudohermaphroditism)

centres appear precociously. The epiphyses fuse earlier than normal and the final height rarely exceeds five feet. The general development is of the male type with broad shoulders and a deep chest. Mental development accords with the patient's true age. Sexual orientation is usually feminine unless the patient has been brought up as a boy, in which case it may be masculine.

Pre-pubertal virilism in the female is caused more often by a tumour than by hyperplasia. During childhood a previously normal infant develops signs of virilism and abnormalities of skeletal growth, similar to those seen in female pseudohermaphroditism.

Macro-genitosomia praecox is precocious development of secondary sex characters in the male. In the congenital form it is caused by hyperplasia and is analogous with

Female pseudohermaphroditism is congenital and is always the result of hyperplasia. It is often familial, but not hereditary. Male members of the same family may have macrogenitosomia præcox. Two main types of maldevelopment of the external genitalia may be found at birth, depending on the stage of fœtal life at which the adrenal lesion appears. (1) If the disorder starts between the twelfth and twentieth week the urogenital sinus fails to differentiate into its urethral and lower vaginal components and the urethra and vagina open into a common orifice in a groove on the ventral surface of the clitoris. The uterine tubes, uterus and upper vagina, which develop earlier, are usually normal, but may be atrophic. The ovaries are usually normal in infancy but develop atretic follicles and fail to ovulate at puberty. The clitoris and labia majora enlarge and the labia minora remain small, giving the appearance of a hypospadic penis, and there may be confusion about the determination of sex. The enlargement of the clitoris continues after birth. (2) If the disorder starts after the twentieth week of fœtal life the vagina and urethra develop normally and enlargement of the clitoris is the only abnormality.



FIG. 189. Adreno-genital syndrome in a woman of 29. Note the masculine appearances and hirsutism of the face and chest.

At birth the greatly enlarged adrenals are sometimes palpable. Later, glucocorticoid

undertaken, and the problem is to decide which patients require study. Investigations should certainly be undertaken when there is unequivocal evidence of virilism, when symptoms first develop during childhood, when the onset is rapid, when symptoms cause mental distress or when there is sterility.

(1) Urinary steroids. The 17-ketosteroid excretion is the most important single investigation. It is raised in most, but not all, cases and highest with carcinoma. The secretion can be suppressed by hydrocortisone in hyperplasia and in some cases of adenoma, but not in carcinoma. In adrenal hyperplasia pregnanetriol (pregnanediol chromogen), a metabolite of 17-hydroxyprogesterone, is often found in the urine and disappears after suppression by hydrocortisone. An excess of dehydroisoandrosterone (dehydroepiandrosterone), the main member of the "β-fraction" of the 17-ketosteroids, is often present in cases of tumour and may be simply detected. The 17-ketogenic steroid excretion is usually normal, but may be slightly raised in hyperplasia, since 17-hydroxyprogesterone and its derivatives are included in this steroid fraction. The 17-hydroxycorticoid excretion is usually normal or raised in cases of tumour and normal or low in hyperplasia.

(2) Radiology. There is often precocious development of the ossification centres and fusion of epiphyses in the congenital and pre-pubertal types. This is easily recognized in the wrist joints. X-rays of the adrenals may show hyperplasia or a tumour.

(3) Chromosomal sex determination. In pseudohermaphroditism the patient's "chromosomal sex" may be determined by the presence or absence of the sex chromatin in the nuclei of the skin epidermis (obtained by biopsy). Chromosomal females are "chromatin positive" and males "chromatin negative."

(4) Examination of the persistent urogenital sinus with a urethroscope may help in finding the vaginal opening in pseudohermaphrodites. The internal urethral orifice is normal, but the verumontanum is absent and a large vaginal orifice may be seen near where the external sphincter should be. If the instrument is then passed into the vagina the uterine cervix may be seen and catheterized. Finally, salpingography will confirm the presence of the uterus and tubes. X-rays, following the injection of radio-opaque liquid into the urogenital sinus, will provide similar, but less exact information.

(5) Biopsy of the gonads, which usually involves laparotomy, is rarely necessary.

Differential Diagnosis

In the female the post-pubertal type of the adreno-genital syndrome must be distinguished from four other conditions: (1) "*Simple hirsutism*" cannot always be differentiated from pathological hirsutism, especially when it is accompanied by poorly developed breasts and scanty periods. If, after full investigation, there is doubt about the diagnosis and the condition requires treatment, a therapeutic trial with cortisone (see later) is worthwhile. (2) The *Stein-Leventhal syndrome* occurs in young women and is associated with bilateral polycystic disease of the ovaries, hirsutism, secondary amenorrhœa, sterility and sometimes obesity. The ovaries are palpable on pelvic examination in about half the cases. The 17-ketosteroid excretion is normal or slightly raised. (3) Rare *virilizing tumours of the ovaries* include arrhenoblastoma and luteoma (masculinovoblastoma), both of which are usually palpable and may cause an increase in 17-ketosteroid excretion; tumours of para-ovarian adrenal rests, which have the same biochemical features as those in the normal adrenal sites; and the small Leydig or hilar cell tumour.

pseudohermaphroditism in the female. In childhood it is usually caused by a tumour. The signs are those of a precocious puberty, except that the testes and prostate do not develop and spermatogenesis does not occur, since there is no excessive secretion of gonadotrophin by the pituitary. Rarely the presence of hyperplastic adrenal tissue in the spermatic cord may simulate testicular development. The enlargement of the penis may be great, even in infancy, and erections are frequent. Adrenal insufficiency may develop and skeletal and muscular growth is precocious, as in female pseudohermaphroditism. The term "infant Hercules" is sometimes aptly used to describe the condition.

Investigations

There are two main questions to be answered: "is this a case of the adreno-genital syndrome?" and if so, "what is the underlying adrenal lesion?"



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lesions

The syndrome varies greatly in its severity and manifestations. At one extreme there may be only mild hirsutism or oligomenorrhœa, while at the other there is fully developed virilism. A diagnosis may be made with fair certainty if elaborate investigations are

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Investigations

There are two main questions to be answered: "is this a case of the adreno-genital syndrome?" and if so, "what is the underlying adrenal lesion?"



FIG 191 Precocious osseous development in a boy aged 2 with "constitutional" precocious puberty All the carpal ossification centres are present, including that of the pisiform which usually appears at about 11 The same condition is seen with congenital and pre-pubertal virilizing adrenal lesions

The syndrome varies greatly in its severity and manifestations. At one extreme there may be only mild hirsutism or oligomenorrhœa, while at the other there is fully developed virilism. A diagnosis may be made with fair certainty if elaborate investigations are

girls and adults ovulation, menstruation and breast development occur within a few months, and pregnancy may become possible. If hirsutism is established its further progress is checked, but regression rarely occurs. The testes develop normally in boys. If the epiphyses have fused when treatment is started there can be no further skeletal growth. The blood pressure (when raised) is usually restored to normal.

Plastic surgery may be needed to correct deformities of the genitalia, but should be postponed until the child is 2–4 years old. In female pseudohermaphroditism the clitoris may remain large and should be amputated. Construction of a vagina is necessary in patients with a persistent uro-genital sinus.

Females who are misdiagnosed and brought up as males constitute a special problem. The outlook is usually male and no cortisone should be given. It may be possible to construct a "penile" urethra, but the patient will be sterile. Rarely, the outlook is female and a "change of sex" may be justifiable. This involves treatment with cortisone, suitable plastic surgery and help with the necessary psychological and social re-adjustment.

MIXED CUSHING'S AND ADRENO-GENITAL SYNDROMES

It is not uncommon to find some features of both Cushing's syndrome and the adreno-genital syndrome in the same patient. For example, virilism may be accompanied by hypertension or associated with diabetes, as in the "diabetes of bearded women" described by Achard and Thiers. If a tumour is present it should be removed. If there is no tumour the clinical and biochemical features must be assessed carefully before deciding on the form of treatment. The deciding factor should be the nature of the alteration in protein metabolism. Catabolism, characteristic of Cushing's syndrome, indicates the need for adrenalectomy, while anabolism, which is found in the adreno-genital syndrome, suggests that suppression of the pituitary by cortisone will be effective. In doubtful cases cortisone therapy, controlled by measurement of the 17-ketosteroid excretion, should be tried first.

FEMINIZATION IN THE MALE

This is excessively rare and is caused by an œstrogen-secreting carcinoma. Nearly all cases develop after puberty.

Enlargement of the breasts is constant and there may be atrophy of the testicles, depression of libido, decrease of hair in the male distribution, and obesity. A tumour is usually palpable.

There may be increased excretion of 17-ketosteroids and dehydroisoandrosterone in the urine Oestrogen excretion may be high, but its estimation is laborious.

Other conditions which may cause breast enlargement in the male include puberty, liver disease (especially cirrhosis), œstrogen therapy (for prostatic carcinoma), chorion epithelioma of the testis, adequate feeding following a period of severe undernutrition, and Klinefelter's syndrome (hyalinization of the seminiferous tubules).

A tumour should be removed, if possible, but the prognosis is bad.

PRIMARY HYPERALDOSTERONISM (CONN'S SYNDROME)

This rare condition is caused by an adrenocortical adenoma, or occasionally carcinoma or hyperplasia, which probably excrete excessive amounts of aldosterone.

Laparotomy is usually necessary to establish the diagnosis. (4) The distinction from *Cushing's syndrome* has already been discussed, but intermediate forms are common.

Female pseudohermaphroditism must be distinguished from *male pseudohermaphroditism* and *true hermaphroditism*, in both of which the external genitalia, genital organs and secondary sex characters may be of mixed type. In neither of these is there an excess of 17-ketosteroids nor any pregnanetriol in the urine, and in both the skeletal development is normal. In the male type the chromosomal sex is male and gonadal biopsy reveals testes. In the true type, which is exceptionally rare, the chromosomal sex is either male or female and both testicular and ovarian tissue are present.

Macrogenitosomia præcox must be distinguished from *precocious puberty* which may be "constitutional" or associated with a tumour of the third ventricle. The testicular size and spermatogenic activity correspond with the degree of development of the penis and secondary sex characters. The 17-ketosteroid excretion is normal for the "sexual age" of the patient. Brain tumours may cause neurological signs. Rare virilizing *testicular tumours* include teratomata, interstitial cell adenomata and tumours of adrenal rests. They are usually palpable and may be identified by biopsy. True testicular tumours cause an increase in 17-ketosteroid excretion, particularly of the α-fraction, and sometimes in gonadotrophin excretion, which gives a positive Aschheim-Zondek reaction. Tumours of adrenal rests probably behave like those in the normal sites.

Treatment

The treatment depends on the nature of the adrenal lesion. A tumour requires surgical removal, while hyperplasia is treated with cortisone, which inhibits the production of corticotrophin and supplies glucocorticoid. Resection of hyperplastic adrenal tissue has yielded variable results in the past and is now rarely done. If the presence of a tumour cannot be excluded after full investigation, two courses are possible. If the condition is long-standing, a trial of cortisone therapy may be given for a few months. If the onset has been rapid, surgical exploration should be undertaken.

It matters little which gland is explored. If a tumour is found, it is removed. If the adrenal is hyperplastic it is most unlikely that there is a tumour in the other gland, but if it is normal the other side may require separate exploration. Normal and hyperplastic glands are examined by biopsy, but are not removed.

In hyperplasia cortisone is given intramuscularly for the first week or two in a daily dosage of 100 mg. in adults and older children or 25 mg. in infants. The 17-ketosteroid excretion falls rapidly to normal and the cortisone can then be given by mouth. The oral maintenance dosage for adults is 37·5–75 mg. per day, and for infants 12·5–25 mg., in 3 or 4 divided doses. The individual requirement must be gauged by the clinical response and by the 17-ketosteroid excretion, which should be maintained at about 5 mg. per day for adults and 1 mg. per day for infants. Cortisone is continued indefinitely, but it may be possible to stop it after about 2 years in some cases. In females stilbœstrol is rarely required as well as cortisone. Infants who suffer adrenal crises may require sodium chloride and deoxycortone in addition.

The results of treatment by removal of a tumour or by cortisone suppression depend on the age and development of the patient when treatment is started. In infants development becomes entirely normal. In older children abnormal development is checked and, in girls, female secondary sexual characters appear normally at puberty. In post-pubertal

PHYSIOLOGY

Like the cortex the medulla is an organ of internal secretion, but it is not essential to life. It secretes two catechol amines whose production is under nervous control. The main one is adrenaline which is chiefly concerned with the emergency reactions of "fight or flight." Adrenaline causes tachycardia, increases the metabolic rate, accelerates glycogenolysis in the liver and causes mental excitement and anxiety. The other catechol amine, nor-adrenaline, is the adrenergic nerve transmitter; it causes peripheral vasoconstriction and is concerned mainly with the regulation of blood pressure. It slows the heart and has much less marked metabolic and nervous actions. These differences account in part for the variable symptoms of hyperfunctioning lesions of the medulla and render nor-adrenaline a much more satisfactory therapeutic agent for correcting the hypotension which may follow, for example, adrenalectomy.

These secretions are largely metabolized in the tissues, but small and fairly constant fractions are excreted in the urine, where their measurement is of great value in the investigation of hyperfunctioning lesions of the medulla.

PATHOLOGY

The only lesions of importance are tumours, which may be classified as follows:

A. With Disturbance of Endocrine Function

Increased secretion: Phæochromocytoma.

B. Without Disturbance of Function

Phæochromocytoma,
Ganglioneuroma (benign),
Neuroblastoma (sympathicoblastoma) (malignant).

PHÆOCHROMOCYTOMA (chromaffin tumour)

Pathology

This is an uncommon tumour, usually benign, occurring at all ages, but most frequently between 20 and 50, equally common in the two sexes and occasionally familial. It is bilateral in at least 10 per cent of cases and may occur in chromaffin tissue elsewhere in the retroperitoneal tissues, thorax or neck. The tumours are usually under 5 cm. in diameter, but may be larger. They are round or ovoid in shape and, although well circumscribed, are rarely encapsulated. The smaller ones are surrounded by a thin layer of cortex. Their structure is homogeneous but large tumours may undergo necrosis. Their colour is grey or brownish and they are stained dark brown by chromium salts (chromaffin reaction).

Histologically the tumours resemble adrenal medullary tissue, but the cells vary considerably in size, shape, and definition. The nuclei are often multiple and vacuolation of the cytoplasm is common. Chromaffin staining is always present, but is variable in intensity. Malignant cases have been reported in which metastases were present in the para-aortic lymph glands, liver, lungs, and elsewhere.

The clinical features are intermittent muscular pains, cramps, weakness and paralysis, polyuria and nocturia, hypertension and sometimes pins-and-needles and tetany. There is no œdema, but the reason for this is not clear. Investigation reveals albuminuria, hypokalæmia, mild hypernatræmia, alkalosis, an excess of potassium in the urine and *inability of the kidney to secrete an acid urine after the administration of ammonium* chloride. Aldosterone can be estimated only in special centres and an excess cannot be always recognized in the blood and urine. X-rays may show a tumour.

Treatment consists of correction of the potassium deficiency (which may cause a further rise in the blood pressure) and surgical removal of the tumour or of hyperplastic glands. Considerable improvement may be expected, but some features of the established disease are probably caused by nephrosclerosis and are irreversible.

CORTICAL TUMOURS WITHOUT ENDOCRINE ACTIVITY

Adenomata are not recognized in life unless they are found *incidentally during operations.*

Carcinomata may cause pyrexia, local pain or swelling, fatigue and loss of weight, and their secondary deposits may give rise to symptoms. They may be demonstrable radiologically, but cause no biochemical disturbance. They should be removed surgically, if possible, but the prognosis is bad.

ADRENAL CORTICAL INSUFFICIENCY IN GENERAL SURGERY

Patients suffering from adrenal insufficiency are unable to respond normally to stress by the secretion of cortical steroids. If they suffer injury or infection or *undergo even* minor surgery they are likely to develop acute adrenal failure which may prove fatal. This state of affairs may be encountered in Addison's and Simmond's diseases, in virilizing adrenal hyperplasia, in patients who have previously been subjected to adrenalectomy or hypophysectomy, after the termination of cortisone or corticotrophin therapy, and in certain other conditions associated with toxæmia and malnutrition.

The clinical features of acute adrenal failure are similar to those which may follow adrenalectomy (see later). The first sign may be severe prolonged hypotension following operation in a patient whose adrenal function has not previously been questioned. Adrenal failure should be suspected in such patients if there is no other obvious cause such as bleeding, dehydration, coronary thrombosis, pulmonary embolism or peritonitis.

Patients whose adrenal function is known to be potentially defective, and who require surgery, should be given supportive therapy in the same way as those undergoing adrenalectomy. If Addison's or Simmond's disease is suspected on clinical grounds, and time permits, adrenal cortical function should be fully investigated. If time is short, it is better to give supportive therapy than to withhold it. Those in whom adrenal failure is first suspected post-operatively must be treated immediately with hydrocortisone and (if necessary) nor-adrenaline intravenously and with cortisone and deoxycortone intramuscularly.

ADRENAL MEDULLA

The adrenal medulla is a specialized part of the sympathetic nervous system and is composed of chromaffin cells and some sympathetic ganglion cells. It is richly supplied with non-medullated nerve fibres, derived from the splanchnic nerves.

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Many of these tumours secrete large amounts of adrenaline and nor-adrenaline, which are responsible for the clinical features and which may be detected in the urine and in the tumours themselves. The metastases from malignant tumours may be functionally active.

Clinical Features

The symptoms are variable, depending on the relative proportions of adrenaline and nor-adrenaline which are produced and on whether their secretion is intermittent or continuous. Three main syndromes are recognized.

Sustained hypertension develops in most cases and is probably caused mainly by nor-adrenaline. The blood pressure may rise progressively from the beginning or become permanently raised only after rising intermittently for a period. The acute symptoms as a rule are milder than those of the intermittent syndrome. The condition may be clinically indistinguishable from essential or malignant hypertension.

Intermittent hypertension, probably caused by both hormones, is uncommon. Paroxysms of hypertension (systolic and diastolic) occur at intervals, accompanied by any of the following: anxiety, tachycardia and palpitations, weakness, tremor, headache, sweating, circum-oral pallor, pre-cordial and epigastric distress, coldness of the extremities and paræsthesiæ, nausea, vomiting and diarrhœa, dilatation of the pupils and blurring of vision. The blood pressure may rise to 300 mm. Hg. or more and death from cerebral hæmorrhage, pulmonary œdema, heart failure or circulatory collapse may follow. The paroxysms last for minutes or hours and may come on several times a day or only at intervals of weeks or months. They may arise spontaneously or be precipitated by emotion, exercise or pre-prandial hypoglycæmia. The condition must be distinguished from anxiety neurosis.

The metabolic syndrome, caused mainly by adrenaline, causes symptoms and signs very similar to those of hyperthyroidism. The hypertension is often mild, but is unlike that of hyperthyroidism in that the diastolic pressure is raised. Intermittent glycosuria is common and the basal metabolic rate is increased. The uptake of radio-active iodine is normal.

The patients are usually thin and the tumour can be palpated in about one-third of cases. Pressure on the tumour may provoke a hypertensive attack. Rarely there are multiple subcutaneous neurofibromata.

Investigations

The diagnosis is confirmed by four types of investigation.

Provocative tests are designed to precipitate a paroxysm of hypertension in patients whose blood pressure is normal or only slightly raised. Several drugs have been used, but all are apt to give false positive and false negative reactions. The best is histamine. Before the test the patient should have no sedative for at least 12 hours and no thiocyanate for at least 4 days. A cold pressor test is performed first, the blood pressure being recorded before and for 10 minutes after immersion of the hands in iced water. After the pressure has returned to normal, an intravenous injection of histamine (0·025 mg. of the base) is given rapidly. Within 30 seconds this usually causes flushing, headache, and a slight fall in blood pressure. A subsequent rise in the pressure, greater than that obtained in the cold pressor test and reaching a maximum within 3 minutes, is highly suggestive of

phæochromocytoma. If the pressure rises alarmingly, phentolamine (5 mg.) should be injected intravenously. A smaller rise, occurring later, may be encountered in some people with a labile blood pressure.

Lytic tests are designed to lower the blood pressure during paroxysms or in the state of sustained hypertension. No sedative or thiocyanate should be given beforehand. The best drug is phentolamine (rogitine), 5 mg. of which are injected intravenously over a period of 1 minute. In phæochromocytoma the systolic pressure usually falls at least 35 mm. Hg. and the diastolic pressure at least 25 mm. Hg. for 5 minutes or longer. Normal people and other hypertensives usually sustain a much smaller fall, but false positive results may occur.

Excretion of catechol amines. The 24-hour excretion of adrenaline and nor-adrenaline in the urine may be measured and forms the most reliable method for the diagnosis of phæochromocytoma. The estimation, however, is difficult and should only be performed if the other tests are suggestive of the presence of a tumour. No drugs of any sort should be given for at least 2 days before the test and, if possible, the collection should be started immediately after a hypertensive attack. Normal subjects excrete less than 50 μg. of "nor-adrenaline equivalent" in 24 hours. In essential hypertension the excretion may reach twice this level, while in phæochromocytoma it is 4–50 times greater than normal.

Radiology, by the methods which are used for detecting adrenocortical tumours, may be helpful. Insufflation of gas may precipitate a hypertensive attack and phentolamine should be available for its control. X-rays of the chest are essential, since tumours are occasionally found there.

Treatment

The tumours should be removed without delay since the prognosis is bad. In addition to the measures required for any form of adrenalectomy (see later) the blood pressure requires careful control with drugs. Before operation, if hypertension is sustained, phentolamine (50 mg. by mouth or 5 mg. intramuscularly, every 3–6 hours) should be given. During the operation the blood pressure is recorded frequently, since the induction of anæsthesia or the handling of the tumour may cause it to rise steeply. If it does rise phentolamine (5 mg. per 100 ml. of 5 per cent glucose solution) is infused intravenously at a rate which is determined by the response. After removal of the tumour the pressure may fall abruptly and is then controlled with nor-adrenaline. Substitution therapy with cortical hormones need only be given for bilateral tumours.

If a large tumour has been located in one adrenal, it is best approached by the thoraco-abdominal route. The other gland and the whole abdomen should be palpated carefully at the same time. Otherwise, since the patients are usually thin and the tumours may be bilateral or in ectopic situations, an anterior approach is advised. When a tumour is found it is handled gently to avoid squeezing pressor agents into the circulation, and its vessels must be ligated and divided early. As much adrenal cortical tissue as possible is preserved.

Results of Surgical Therapy

Provided the blood pressure is carefully controlled the operative mortality is low. The results of surgery are good. Paroxysms stop, the metabolic disorders disappear and sustained hypertension is greatly reduced in most cases. If the symptoms and signs

Many of these tumours secrete large amounts of adrenaline and nor-adrenaline, which are responsible for the clinical features and which may be detected in the urine and in the tumours themselves. The metastases from malignant tumours may be functionally active.

Clinical Features

The symptoms are variable, depending on the relative proportions of adrenaline and nor-adrenaline which are produced and on whether their secretion is intermittent or continuous. Three main syndromes are recognized.

Sustained hypertension develops in most cases and is probably caused mainly by nor-adrenaline. The blood pressure may rise progressively from the beginning or become permanently raised only after rising intermittently for a period. The acute symptoms as a rule are milder than those of the intermittent syndrome. The condition may be clinically indistinguishable from essential or malignant hypertension.

Intermittent hypertension, probably caused by both hormones, is uncommon. Paroxysms of hypertension (systolic and diastolic) occur at intervals, accompanied by any of the following: anxiety, tachycardia and palpitations, weakness, tremor, headache, sweating, circum-oral pallor, pre-cordial and epigastric distress, coldness of the extremities and paræsthesiæ, nausea, vomiting and diarrhœa, dilatation of the pupils and blurring of vision. The blood pressure may rise to 300 mm. Hg. or more and death from cerebral hæmorrhage, pulmonary œdema, heart failure or circulatory collapse may follow. The paroxysms last for minutes or hours and may come on several times a day or only at intervals of weeks or months. They may arise spontaneously or be precipitated by emotion, exercise or pre-prandial hypoglycæmia. The condition must be distinguished from anxiety neurosis.

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ADRENALECTOMY

INDICATIONS

Adrenalectomy is performed for the following conditions:

(1) *Tumours* of the adrenal cortex or medulla (whether functionally active or not). Excision of the tumour may involve removal of all or most of the gland.

(2) *Cushing's syndrome* with hyperplastic or hyperfunctioning adrenal glands.

(3) *Hyperaldosteronism* with hyperplastic glands.

Both glands are removed totally or sub-totally.

The indications for adrenalectomy in these conditions have been discussed already.

(4) *Various conditions* not directly associated with adrenal disorder. Both glands are totally removed with the object of eliminating the cortical secretions which may play a part in the genesis or persistence of disease. The main conditions are metastatic *carcinoma of the breast or prostate* (which may be œstrogen-dependent or androgen-dependent respectively), essential or malignant *hypertension* (in which glucocorticoids and electrocorticoids may play a part) and *diabetes mellitus* (to which glucocorticoids may contribute). The place of adrenalectomy in these conditions cannot yet be finally assessed and it is possible that hypophysectomy may prove a better operation.

SURGICAL APPROACH

The main problem in the surgery of the adrenal glands is that while it is frequently desirable to inspect both glands before removing one, there is no incision which always gives adequate access to both glands at the same time. Various approaches may be employed:

(i) An oblique thoraco-abdominal incision, with resection of a rib, gives excellent exposure of one adrenal. The opposite gland, the ovaries and ectopic adrenal swellings can be palpated via the peritoneal cavity, but they cannot be seen or removed. In thin patients (e.g. with metastatic carcinoma) resection of the 12th rib gives adequate access In those who are fat or who have a large adrenal tumour the *left* gland is best approached extra-pleurally through the bed of the 11th rib, while on the *right* a trans-pleural, transdiaphragmatic incision through the bed of the 10th rib gives the best exposure.

(ii) An anterior abdominal incision allows both glands to be palpated and inspected, and in a thin patient they can be removed. Great difficulty may be experienced, especially on the right side, if the patient is fat or deep-chested, or if a large tumour is present.

(iii) Bilateral para-vertebral incisions, with the patient prone, allow both glands to be inspected at the same time, and resected if necessary. This approach is satisfactory only in experienced hands.

The thoraco-abdominal approach is recommended except for cases of phæochromocytoma, children and thin patients with metastatic carcinoma, for whom an anterior incision is usually better. When two explorations are necessary to examine or resect the adrenals it is generally safer to operate in two stages It may be justifiable to turn the patient after completion of one operation and proceed immediately with the other, but this should not be done if the pleural cavity has been opened, if the patient's condition causes any anxiety or if the surgeon is inexperienced in adrenal surgery. If adrenalectomy and oöphorectomy are being performed for malignant disease, it is reasonable to remove the left gland and the ovaries at one operation, and the right adrenal at another.

persist after removal of a tumour a careful search should be made for another. This may involve a further abdominal exploration.

NEUROBLASTOMA AND GANGLIONEUROMA

Pathology

A typical neuroblastoma consists of immature undifferentiated neuroblasts and is highly maligant, while a typical ganglioneuroma is formed from well-differentiated nerve cells and fibres, and is benign. There are, however, many intermediate forms.

Neuroblastoma, although rare, is one of the commonest malignant tumours of infancy and early childhood, and may be present at birth. It is rare in adults. Ganglioneuroma, on the other hand, is more common in older children and in young adults. The tumours are probably equally common in the two sexes. About one-third of them arise in one or other adrenal medulla, one-third in sympathetic tissue elsewhere in the abdomen and one-third in the thoracic or cervical parts of the sympathetic chains. Multiple primary tumours have been described.

Neuroblastomata usually metastisize early and widely, and the secondary deposits may be much larger than the primary growths. Metastasis to bone is common and new bone formation in the lesions may lead to confusion with Ewing's tumour or osteogenic sarcoma. The name of "Hutchinson's syndrome" was formerly applied to cases in which metastases were prominent in the skull. Metastasis or direct extension to the liver is also common and the term "Pepper's syndrome" was used to describe cases with hepatic enlargement. The lungs and other organs are also frequently involved and lymphatic spread to the para-aortic lymph glands is common.

Clinical Features

Non-specific features such as intermittent abdominal pain or pyrexia may develop early, but a tumour is rarely suspected until a swelling is found on palpation. Secondary deposits may cause symptoms and signs locally.

Investigation

Radiology of the adrenals and the skeleton, biopsy of accessible lesions, aspiration biopsy of the bone marrow and surgical exploration are all valuable.

Treatment

The primary tumour should be removed, if possible. Irradiation of the operation area and of secondary deposits may cause some regression and temporary remissions may be induced by nitrogen mustards and folic acid antagonists.

Prognosis

The prognosis following the removal of benign tumours is good. Malignant tumours may undergo partial remissions spontaneously or as a result of therapy, but the ultimate prognosis is hopeless.

except in the operation scars, and excessive loss of weight are indications for continuing cortisone.

After total adrenalectomy cortisone must be given permanently by mouth, the usual maintenance dosage being 25–50 mg. per day in 3 or 4 divided doses. Some patients with metastatic carcinoma may require up to 100 mg. daily. Until the dosage is stabilized the serum sodium and chloride levels should be measured at intervals. Occasionally they remain low and deoxycortone must be given as well. When the required dosage has been found by daily injections, deoxycortone trimethylacetate (usually about 25 mg.) may be given intramuscularly every 3 weeks and may be supplemented by sodium chloride (2 gm. daily in enteric-coated capsules.)

The necessity of taking cortisone and the early symptoms of its deficiency must be impressed on the patients, and a card with printed instructions, such as the following, may be used:

M..............................

CARRY THIS CARD WITH YOU ALWAYS

1. Your adrenal glands have been removed. It is essential for you to take Cortisone tablets every day, and you will remain in good health if you do so. Your doctor will give you prescriptions for them. Your dose is .. tablets (. . mg) .... times a day.
2. The dose may have to be increased temporarily if you develop an illness (e.g. a bad cold), have an accident or have to undergo an operation (e.g. for appendicitis). Show this card to your doctor or to the hospital doctor at the time.
3. If you feel weak or lose your appetite it may mean that you are not taking enough Cortisone. Try taking an extra half tablet twice daily and see if you feel better. If you don't, go to your doctor at once.

After removal of a functioning tumour in Cushing's syndrome the remaining atrophic adrenal tissue should be stimulated by the injection of corticotrophin-gel. Eighty units are given intramuscularly twice daily for a week, and progressively smaller doses are given for a further week. Substitution therapy is given as well.

Adrenal Insufficiency

Three types of adrenal insufficiency may be encountered:

(i) **Acute peripheral circulatory failure** (adrenal crisis) develops usually within 24 hours of operation and may appear very suddenly. It is commonest after operations for Cushing's syndrome and may not be prevented by substitution therapy. The signs, which are similar to those of oligæmic shock, are tachycardia, hypotension and collapse. If the systolic blood pressure falls below 100 mm. Hg. an intravenous infusion of hydrocortisone should be started immediately. 100 mg. (in 500 ml. of 5 per cent glucose) are given in the first 4 hours, after which the rate is reduced. If the fall is profound or if it continues after starting hydrocortisone, nor-adrenaline should be given as well, using a "two-bottle" transfusion set. A solution containing 4 mg. per 500 ml. of normal saline or 5 per cent glucose is given as fast as necessary to restore the blood pressure. The response is usually immediate and the rate of infusion must be adjusted every few minutes. Withdrawal of nor-adrenaline must be slow. A rare complication is superficial gangrene which appears

PRE-OPERATIVE AND POST-OPERATIVE CARE

General Measures

The patient is kept ambulant up to the day of operation and breathing exercises are started. A "broad-spectrum" antibiotic is given from the time of operation, since cortisone suppresses inflammatory reactions. If acne or other infections are present the antibiotic is started a few days before operation. An intravenous infusion, preferably through a "polythene" tube which is passed well up the long saphenous vein, is started before operation and continued until a normal blood pressure has been maintained for 48 hours without remedial measures. This enables blood, hydrocortisone or nor-adrenaline to be given without delay if they are needed. The patient's blood is cross-matched and blood transfusion is given if necessary. The pulse rate and blood pressure are recorded every 15 minutes after operation until the blood pressure has been stabilized.

Substitution Therapy

The effects of removing adrenal tissue without adequate substitution therapy can be disastrous and many deaths from adrenal failure occurred before cortisone became available. An adrenal crisis may follow removal of one gland only, even in the absence of tumour. It is *essential* to give adrenal cortical hormones over the period of operation when bilateral adrenalectomy is proposed or when a functioning tumour is to be removed. It is *wise* to provide substitution therapy when exploring or removing adrenal tissue for any cause. It should also be given for *any operation* on patients whose adrenal function may be defective, especially after adrenalectomy and during or after cortisone therapy (see above).

The following scheme of dosage for cortisone and deoxycortone is satisfactory:

Day	Cortisone Acetate	Deoxycortone Acetate
2 days before operation	50 mg 6-hourly, i m	
1 day before operation	50 mg 6-hourly, i m	
Day of operation	100 mg 3 hours before operation, by mouth 25 mg 6-hourly, i m	10 mg. 3 hours before and 5 mg 6 hours after operation, i m
1 day after operation	25 mg 6-hourly, by mouth if possible, otherwise i m	5 mg 12-hourly, i m
2–5 days after operation	25 mg 6-hourly, by mouth if possible, otherwise i m	5 mg i.m.
6–10 days after operation	12 5 mg 6-hourly, by mouth	
11+ days after operation	12 5 mg b d , by mouth	

If, for any reason, pre-operative preparation has not been given, the above schedule is started at the time of operation and *hydrocortisone* is given instead of the pre-operative cortisone. About 300 mg. in 1500 ml. of 5 per cent glucose solution is given intravenously during the first 24 hours, the infusion being stopped slowly when the blood pressure is being maintained at a normal level.

After sub-total adrenalectomy the cortisone is withdrawn gradually and can often be stopped after a few weeks or months. The required dosage is determined by the absence of signs of adrenal failure when trial reductions are made. Addisonian pigmentation,

over the outer border of the sacro-spinalis muscle and extended along the line of the 11th or 12th rib (whichever is chosen) well into the abdominal wall. The rib and abdominal muscles are exposed and the rib resected subperiosteally as far back as its angle. The abdominal muscles and lumbar fascia are incised and the intercostal or sub-costal nerve and vessels are carefully preserved. The bed of the rib is incised and the diaphragm divided, taking care to avoid the pleura. If the pleural cavity is opened inadvertently

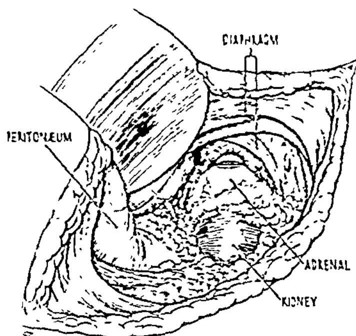


FIG. 192. The crucial stage in left-sided sub-total adrenalectomy. The adrenal has been approached via the bed of the 11th rib and exposed on its anterior and lateral aspects. The upper pole has been divided without disturbing the deep surface of the gland.

the lung must be inflated before the incision is closed. Retractors are inserted, the kidney found by palpation and the renal fascia incised. The kidney is retracted downwards and the adrenal identified at its upper pole. The inexperienced may easily mistake the tail of the pancreas for the adrenal. The peritoneal cavity is opened in front of the colon and the ovaries and opposite gland are palpated. If sub-total removal is proposed, the lateral and anterior aspects are cleared without disturbing the gland posteriorly or injuring the small vessels which enter its periphery, and a small corner—not more than one-tenth of the whole—is selected to be left in the body. The upper pole is usually suitable and is severed from the main portion of the gland with scissors. If it is viable its colour remains unchanged and blood oozes from its cut surface. If it is not viable the process is repeated with another corner. The remainder of the gland is then removed and the vein, which usually passes down from its medial aspect to the renal vein, is ligated and divided. If total adrenalectomy is proposed, the gland is removed in one piece. After hæmostasis has been secured the table is straightened and the incision closed with interrupted sutures. The main layer is the rib bed behind and the lumbar fascia in front. The superficial muscles are sutured and the skin closed. Drainage is not usually required.

rapidly near the site at which the nor-adrenaline enters the vein. Pallor may be recognized early in these cases and gangrene prevented by injecting acetyl choline (100–200 mg.) locally. If the gangrene is extensive it must be treated by excision and grafting.

(ii) **The cortisone withdrawal syndrome** develops if the cortisone dosage is reduced too rapidly after operation or if, as a result of stress, the patient's cortisone requirements increase. The first symptoms are early morning anorexia and nausea, induced by ambulation and eased by rest. The nausea becomes persistent and is followed by vomiting and dehydration. There is bodily weakness and a feeling of uneasiness or actual pain in the abdomen. The signs are tachycardia and an irregular low-grade fever, followed later by hypotension, which may cause oliguria and anuria. The patient's mental attitude may change from one of ready co-operation to that of surly truculence. In Cushing's syndrome the usual desquamation of the skin is accentuated. The condition, which may be fatal if it is not treated, responds at once to an increase in the dose of cortisone. If vomiting is severe, hydrocortisone should be given intravenously.

(iii) **Acute salt deficiency** is rare. Apathy, nausea and weakness are associated with a low concentration of sodium in the serum. It may be corrected by giving sodium chloride (as a 10 per cent solution) intravenously.

Post-operative Complications

Apart from adrenal insufficiency, the pulmonary and other complications of any thoracotomy or laparotomy may develop and must be treated. Wound infection and dehiscence are not uncommon, probably as a result of cortisone therapy or previously existing hyperadrenocorticism. They are treated by specific antibiotic therapy and, if necessary, by drainage of an abscess or re-suture of the incision.

SURGICAL TECHNIQUE

General Considerations

General anæsthesia is used with a cuffed endo-tracheal tube. Great care should be taken to adjust the patient's position on the operating table so that the exposure is as good as possible. The upper pole of the kidney is the best guide to the adrenal on each side and the gland is recognized by its orange colour. The adrenals are friable and if cells are spilled they may regenerate. To avoid this they are handled as little as possible with the forceps and are removed with a thin covering of fat. They may be mobilized by blunt and sharp scissor dissection. In the absence of a tumour, bleeding is rarely troublesome and usually the vein on each side is the only vessel which requires ligation. The small vessels can be sealed with diathermy. Tumours, particularly carcinomata, may have many additional vessels which must be ligated as they are encountered before the tumour is removed. Gross invasion of the surrounding tissues may make their removal impossible, but removal of the kidney and the spleen (on the left) may enable the whole tumour to be excised. A careful search should always be made for ectopic adrenal tissue near the main glands.

Left Adrenalectomy

The patient is placed in the lateral position with the left side uppermost and the table is well "broken" with its apex under the line of the incision. A straight incision is started

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Right Adrenalectomy

The lateral position is again used. If the 11th or 12th rib incision is used the procedure is the same as that on the left side. With the higher incision the 10th rib is resected from its angle to the costal margin and the pleural cavity is opened. The ribs are held apart with a self-retaining retractor, the right kidney is palpated and the diaphragm is incised over it in the line of the skin incision. The liver is held forwards with a retractor, the renal fascia is incised and the adrenal located at its upper pole. The gland is cleared on its anterior aspect and the vein (or veins), which enter the vena cava directly, are found, ligated with the aid of an aneurysm needle and divided. If this step is not undertaken early in the operation there may be serious bleeding. The gland is then removed, hæmostasis secured and the diaphragm sutured. The incision is closed in the same way as that on the left, taking care to inflate the lung.

Bilateral Adrenalectomy by the Abdominal Route

The patient is placed supine and the table is "broken" under the twelfth thoracic vertebra. A long mid-line upper abdominal incision is made and, if necessary, is extended laterally in either or both flanks. Lateral tilting of the table first to one side and then to the other assists the exposure of the glands. The right adrenal is approached by retracting the liver upwards and mobilizing the duodenum towards the left and the hepatic flexure of the colon downwards. The left adrenal is exposed by mobilizing the splenic flexure of the colon downwards and retracting the spleen, stomach, and tail of the pancreas upwards and to the right. On each side the kidney is retracted gently downwards and the peritoneum incised just above its upper pole. The adrenals are exposed fully and examined by inspection and palpation. Finally, a careful search is made throughout the para-aortic region and pelvis for ectopic tissue. When the adrenal tissue has been removed the incision is closed in layers. Drainage is usually unnecessary.

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2 glands in 1 case, 3 in 26 cases, 5 in 25 cases, and 6 in 2 cases, of a series of 428 dissections.

The superior parathyroids are found on the posterior border of the inner surface of the thyroid gland, somewhere above its lower third in 90 per cent of cases (Gilmour, 1938). The inferior parathyroids lie near the lower third of the posterior border of the thyroid in relation to a terminal branch of the inferior thyroid artery, or they may lie just below the lower pole of that gland. One of the inferior parathyroids may be in an aberrant position, lying some distance below the lower pole of the thyroid in the fatty tissue of the neck or in the fat of the anterior mediastinum where it may lie in front of the thymus gland or low down in the mediastinum as far as the arch of the aorta (Gilmour, 1938). An inferior parathyroid gland rarely lies within a lobe of the thyroid gland near its lower pole; sometimes its location in a deep groove on the surface of the thyroid may be mistaken for a true intra-thyroid gland.

The parathyroid may be easily visible and recognizable by its colour or it may be partly surrounded by fat through which its small, vascular pedicle passes. The artery for the superior parathyroid gland comes from the inferior thyroid artery or from an anastomotic channel between the superior and inferior thyroid arteries; that for the inferior glands comes from the inferior thyroid artery.

PHYSIOLOGY

The principal function of parathormone seems to be to control the level of the serum calcium. With excess of circulating parathormone, as in hyperparathyroidism, the serum calcium is elevated and the serum phosphorus is reduced and there is hypercalciuria and hyperphosphaturia. In hypoparathyroidism these changes move into reverse. The precise mechanism of the action of parathormone is not completely clear.

Collip *et al.* (1925) suggested that the primary action of parathormone was to cause a stimulation and multiplication of osteoclasts; the resulting resorption of bone, liberated calcium and phosphorus into the blood stream. This theory explains the elevated serum calcium levels in hyperparathyroidism but does not explain the low serum phosphorus levels which are usually present. An alternative theory is that of Albright (Albright and Reifenstein, 1948) who believed that the primary action of parathormone was on the renal tubules which were rendered more permeable to phosphate; there was a consequent decrease in the serum phosphorus levels. The reduction in serum phosphorus resulted in the mobilization of calcium phosphate from the bones in order to preserve the normal calcium-phosphorus product. Under such circumstances the serum calcium was raised with a resulting hypercalciuria; the maintenance of the elevated serum calcium resulted in a slow but continuous dissolution of bone.

The evidence as a whole reviewed by Dent (1953), suggests that the action of parathormone is two-fold. There is a principal action whereby the osteoclasts are stimulated, with a resulting liberation of calcium and phosphorus from the bone and a hypercalcæmia and hypercalciuria; there would in consequence be a hyperphosphatæmia unless the subsidiary action of the hormone came into play, which is to increase the renal phosphate clearance, resulting in a hyperphosphaturia and hypophosphatæmia.

The amount of the parathyroid hormone that is required to achieve normal blood calcium levels varies under certain circumstances; thus in pregnancy, lactation, or

CHAPTER XI

SURGERY OF THE PARATHYROID GLANDS

L. N. PYRAH

THE parathyroid glands, usually four in number, lie in the neck behind the thyroid gland. Their function is to regulate the level of calcium in the blood by the secretion of parathormone, the active agent. Of surgical interest is the pathological reduction of the total active parathyroid tissue in the body, or the over-production of parathormone by the formation of tumours or because of hyperplasia in the glands. Rarely, malignant changes occur in one of the glands.

HISTORICAL INTRODUCTION

The existence of the four parathyroid glands was first established by Sandstrom (1880) who correctly described their intimate relationship with the thyroid gland. Osteitis fibrosa cystica was first described by Von Recklinghausen (1891), who gave an accurate description of the pathology though he did not suspect the relationship of the disease to the parathyroid. Askanazy (1904) first noted the association of a tumour of one parathyroid gland with osteitis fibrosa cystica though he did not realize its ætiological significance. Erdheim (1907) recorded the relationship of enlargements of the parathyroid glands with some diseases of the bony skeleton. It was not until 1925 that Mandl of Vienna carried out the first removal of a parathyroid adenoma for osteitis fibrosa cystica. He did not at first recognize that the bone disease was caused by hyperparathyroidism but thought on the contrary that a deficiency of active parathyroid secretion may have been the cause; he first, therefore, treated his patient with an extract of parathyroid glands and later he transplanted human parathyroid glands into the patient, a procedure which, he thought, made him worse; exploration of the neck ultimately revealed a parathyroid tumour, after the removal of which the patient made rapid improvement.

Parathormone, the active principle of the gland, was first prepared by Hanson (1925) and also by Collip (1925), who with his co-workers demonstrated the actions of the hormone (Collip, Clark, and Scott, 1925). Albright and his co-workers in Boston have made important contributions to the pathology and the surgery of hyperparathyroidism and in a long series of papers have greatly added to our knowledge on this subject (Albright and Reifenstein, 1948).

SURGICAL ANATOMY

The normal parathyroid gland is ovoid, spheroidal or disc-like, of a yellow-brown colour, weighs from 30–40 mg. (Gilmour and Martin, 1937) and its average dimensions are 6 × 4 × 1·5 mm. (Gilmour, 1938). The parathyroids are normally closely applied to the surface of the thyroid gland or may lodge in a small depression or sulcus of its posterior border. The normal number of glands is four but Gilmour (1938) reported

four parathyroid glands, of multiple adenomata, of primary hyperplasia of all four parathyroid glands or of carcinoma. Single adenoma probably accounts for 90 per cent of all cases. The principal resultant changes are found in the bony skeleton and the kidneys.

Pathology

Single Adenoma. An adenoma may be but little larger than a normal parathyroid gland (approximately 30 mg.) or may weigh several grams. The smallest tumour in the writer's series weighed 65 mg. In the smaller tumours, which are usually spherical or ovoid, a flattened layer of normal parathyroid tissue may be found outside the capsule of



Fig. 193. Normal adult parathyroid The gland is composed of loosely arranged clumps and strands of cells separated by abundant fat (H. & E × 17.)

the adenoma; as the adenoma enlarges it assumes various shapes depending upon its relation to the thyroid gland and to the blood vessels; thus it may be ovoid or tetrahedral or a flattened disc, or it may be hour-glass shaped, being compressed about its centre by the inferior thyroid artery. The tumour may retain its close anatomical relationship to the thyroid gland or it may descend into the fatty tissues of the neck or into the retro-œsophageal space, a vascular pedicle derived from the inferior thyroid vessels serving as a guide to its position. The tumour is brownish-yellow in colour quite different from the bluish tinge of the thyroid gland, and it is surrounded by a delicate areolar capsule; the tumour is occasionally enlarged from cystic change and is firm in consistency because of calcification.

Microscopically, whereas a normal parathyroid is of rather loose texture, the cells or groups of cells being separated from each other by fat (Fig. 193), the adenoma is a dense, compact mass of cells closely applied to each other, the stroma containing little fat. The most common type is the chief-cell adenoma (Fig. 194) and others are the transitional chief-cell adenoma, the transitional wasserhelle-cell adenoma and the functionless oxyphil-cell adenoma; apart from the last-named, no relationship has been discovered between the clinical symptoms and the pathological variants of the tumour.

Multiple Adenomata were found in 20 of 322 cases collected by Norris (1947) from the world's literature.

calcium deprivation in the diet, the need for more of the hormone by the body leads to *hypertrophy of the glands, which may be regarded as physiological.*

HYPOPARATHYROIDISM

Idiopathic hypoparathyroidism has been described. Five cases of this condition associated with moniliasis were reported by Sutphin, Albright, and McCune (1943), three of the cases occurring in siblings. Idiopathic hypoparathyroidism may be associated with Addison's Disease (Leonard, 1946).

Surgical removal of, or injury to the parathyroid glands during the operation of subtotal thyroidectomy is the commonest cause of hypoparathyroidism; in cases in which there is injury to their blood supply, normal activity of the glands may return after some months.

Symptoms. When all the parathyroid tissue in the body has been removed the serum calcium falls to a very low level and symptoms of tetany occur; subtotal removal may result in the appearance of some of these symptoms. Tingling in the fingers and toes with numbness of the extremities are early symptoms while the more severe ones are carpo-pedal spasms, cramps in the limbs, laryngeal stridor, and convulsions. Tetany from laryngeal spasm may, rarely, be fatal. Cataract is a common complication. The skin may be dry, coarse and scaly and the hair on the head and eyebrows, the axillæ and the pubic regions scanty.

Physical Signs and Diagnosis

Tapping over the facial nerve in front of the tragus results in an immediate twitch of the muscles of the upper lip and the angle of the mouth (Chvostek's sign). Trousseau's sign is demonstrated by inducing carpo-pedal spasm by means of reducing the circulation of a limb by raising the pressure in the rubber cuff of a sphygmomanometer; in the arm the wrist becomes flexed and the fingers flexed at the metacarpophalangeal joints but extended at the interphalangeal joints. The test should be positive after keeping the pressure in the cuff above that of the normal blood pressure for 3 minutes. The serum calcium may fall below 7 mg. per 100 c.c. and at such levels calcium is usually absent from the urine if examined by the Sulkowitch test (Albright and Reifenstein, 1948).

Treatment. In mild cases the administration of calcium gluconate by mouth or intramuscularly relieves the tingling of the fingers, allays apprehension and restores a sense of well-being, injections of parathormone are less effective. In long-standing or permanent hypoparathyroidism, in addition to administering calcium by mouth, the serum calcium levels must be restored to normal by the administration of dihydrotachysterol or A.T. 10, or alternatively by injections of parathormone. Doses of 3 c.c. of A.T. 10, which increases the amount of calcium absorbed from the intestine and also the urinary excretion of phosphate, are given daily until the serum calcium is raised to normal and calcium re-appears in the urine The exact dose, which may then be reduced to a maintenance dose of 1–2 c.c. daily, must be determined following repeated serum calcium estimations as well as the disappearance of the clinical symptoms of hypoparathyroidism. Calcium by mouth as well as a high calcium diet must be given indefinitely.

PRIMARY HYPERPARATHYROIDISM

Primary hyperparathyroidism may be the result of a single adenoma of one of the

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Multiple Adenomata were found in 20 of 322 cases collected by Norris (1947) from the world's literature.

Primary Hyperplasia. Enlargement of all four parathyroid glands due to a hyperplasia of wasserhelle cells and resulting in hyperparathyroidism was first described by Albright, Bloomberg, Castleman, and Churchill (1934). The glands usually enlarge unequally, and in appearance, colour, and shape as well as by the frequent presence of cysts and foci of calcification, may mimic multiple adenomata. The total weight of the hyperplastic tissue varies greatly; in Black's series (1953) the weight varied

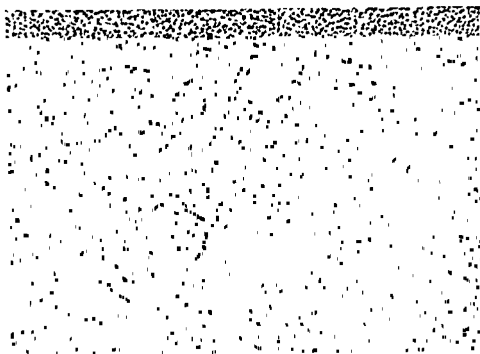


FIG. 194 Parathyroid adenoma composed of a compact mass of large chief cells (H. & E × 160)

from 1·4–52·5 gm Microscopically this form of hyperplasia consists entirely of the so-called water-clear or wasserhelle cells which contain abundant clear cytoplasm with a deeply-staining, often eccentric nucleus; the cells are arranged in groups, separated from each other by a network of delicate fibrous tissue.

The Bones. In the bones lacunar resorption is the most important change, though new bone formation also takes place. In the rarefied areas there is a replacement of the marrow by fibrous tissue and cysts form in foci of degeneration. Osteoclastomata may be found in the jaw or the long bones; these pseudo-tumours consist of large osteoclasts among fibrocytes which are less differentiated than in the remainder of the fibrous marrow; sometimes they are minute foci but the larger ones expand the compact tissue of the bone (Hunter and Turnbull, 1931).

The Kidneys. The kidneys, which frequently contain calculi usually show cellular changes and microscopical calcification. Nephrocalcinosis which is demonstrable radiologically represents a late stage of the microscopic intra-renal calcification seen in the earlier stages of the condition. Calcium salts are deposited in the cells of the renal tubules, sometimes resulting in destruction of the cell body and impregnation of the basement membrane with calcium. The cell body may be extruded into the tubular lumen as a cast. Nephrosclerosis of individual nephrons may occur, leading to widespread sclerotic

changes; such changes in the renal parenchyma will probably be permanent even if the adenoma is removed.

Other Organs. In fatal cases, widespread microscopic calcification may be found in many organs, especially the alveolar epithelium of the lungs, the pancreas and the heart-muscle.

Ætiology

The incidence in the two sexes is approximately the same. Hyperparathyroidism may occur at any age, from the first decade onwards; the youngest case in the writer's series was a girl of fifteen. The disease results in progressive symptoms lasting many years, and many patients with long-standing but relatively mild hyperparathyroidism live to the later decades.

Clinical Symptoms

In the twenty years following the first case of hyperparathyroidism reported by Mandl (1926), although it was known that renal calculi commonly complicated hyperparathyroidism, it was the skeletal symptoms which attracted most attention and which most commonly led to the diagnosis. Although Albright and his co-workers in 1934 had shown that renal calculi alone could be the sole clinical manifestation of hyperparathyroidism, this fact was slow to be recognized and it is only in series published since 1947 that many cases having renal stones alone have been recorded. Since that time it has become increasingly evident that the commonest manifestation of primary hyperparathyroidism is renal calculus or nephrocalcinosis, and that cases having skeletal changes alone are the least common form of the syndrome. A few cases have been reported, probably discovered following routine biochemical tests, of primary hyperparathyroidism having neither skeletal changes nor renal stones.

The attention of surgeons in urological clinics in recent years has been focused upon the diagnosis of hyperparathyroidism in cases of renal calculus especially when these have recurred after removal and also in patients with bilateral calculi, and such cases are being increasingly found. Albright and his co-workers believe that 5–10 per cent of calcium-containing calculi may be the result of hyperparathyroidism. Table I shows the varying proportions of cases of hyperparathyroidism manifesting skeletal changes only, skeletal changes as well as renal calculosis and cases of renal stones alone in some of the larger published series.

TABLE I. PRIMARY HYPERPARATHYROIDISM; PUBLISHED SERIES

	Norris 1947	Albright and Reifenstein 1948	Black 1953	Hellstrom 1954	Pyrah 1934–1955	Total
Skeletal changes alone .	191	11	16	13	13	244
Skeletal changes with nephrocalcinosis or renal calculi . .	101	24	16	10	14	165
Nephrocalcinosis or renal calculi alone	17	28	73	27	10	155
Neither skeletal changes nor calculi .	5	1	7	—	—	13
TOTAL	314	64	112	50	37	577

Some published series of cases of primary hyperparathyroidism; the more recent series have a higher proportion of cases of renal calculi alone.

The factors which determine whether skeletal symptoms preponderate or whether renal stones are the sole manifestation, are probably the size of the tumour and its activity in the production of parathormone, together with the intake of calcium by mouth. Cases with radiologically demonstrable skeletal changes have larger tumours, whereas most of the cases with renal stone alone have smaller tumours some of which are very small. Similarly, in the skeletal group there are often gross biochemical changes in the blood, while in those with renal calculi alone, the changes are but little removed from normal. It is probable that if calcium is lost in the urine in small or moderate amounts in excess of



FIG. 195 Long-standing case of osteitis fibrosa cystica showing severe deformity of the pelvic bones

normal, that such loss can be compensated for by an adequate intake of calcium by mouth; thus, patients with a high intake of calcium-containing foods such as milk and milk-products, may, even in the presence of marked hyperparathyroidism, escape demonstrable skeletal changes though they may develop renal stones consequent upon the hypercalciuria.

Few patients, therefore, develop the complete clinical picture of hyperparathyroidism. The symptoms, however, are conveniently described as those relating to the skeletal system, those relating to the urinary tract and the symptoms due to hypercalcæmia; some associated conditions will also be referred to.

Skeletal Changes. Pains in the limbs and the spine associated sometimes with bone tenderness are common early symptoms. A general sense of weakness, a lack of normal well-being and early fatigue, are usually present. A lump in one bone, such as the lower jaw or the tibia, may reveal the presence of a bone cyst or osteoclastoma. A spontaneous fracture of a long bone or one following trivial violence may be the first symptom and may lead to the diagnosis being made since the fracture may be seen radiologically to have

occurred either in an osteoporotic bone or at the site of a cyst or pseudo-tumour. If the patient escapes these complications, slow deformities may occur, such as a kyphosis leading to diminution in stature or a lordosis following deformity of the pelvis (Fig. 195);



FIG 196 Osteitis fibrosa cystica with fairly extensive cystic change in the upper end of the right femur



FIG 197. Osteitis fibrosa cystica There are multiple cysts in the tibia and one in the centre of the fibula causing expansion of the bone

bending of long bones may occur. The neck may be shortened and thickened. A pigeon-breast deformity of the chest or a forward displacement of the head and the thorax may slowly develop.

In cases with marked skeletal disease, the radiological changes are gross and are very often diagnostic. There is a general demineralization of all the bones of the skeleton;



FIG 198. Long-standing case of osteitis fibrosa cystica. The ribs of both sides, especially the right, have collapsed laterally.

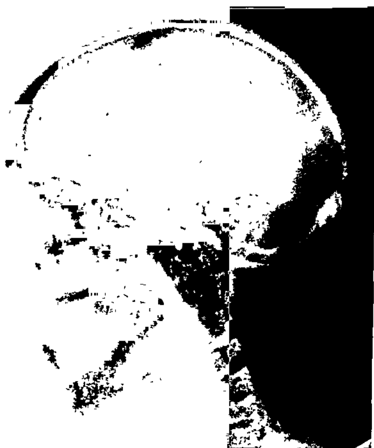


FIG 199. Skull in a case of hyperparathyroidism showing diffuse granular type of rarefaction over the whole of the calvarium.

the compact bone becomes less dense and in advanced cases it can be seen on the radiograph to be reduced to a thin, linear, cortical zone. Cysts may be small in size and few in number or numerous and large (Figs. 196 and 197); they may be present in the long bones, the vertebræ, and the jaws; occasionally, in cystic zones, thin, bony septa remain, giving an appearance which mimics that of osteoclastoma. Cysts are common in the medullary parts of the bones though sub-cortical cysts are found. The vertebræ may become wedge-shaped and crush fractures occur. Coxa vara may replace the normal angle between the body and the neck of the femur. The lateral chest wall may collapse inwards (Fig. 198) giving a well-marked sulcus and the sternum may be pushed forward making the chest barrel-shaped. Early radiographic changes are found in the skull, which then has a ground-glass appearance in the calvarium (Fig. 199); the lamina dura of the teeth are absent. Some of the earliest bone changes, to which Pugh (1951) drew attention, and which may easily be masked in the more fully developed radiological picture, are subperiosteal resorption of bone. Here the outer part of the cortex of certain bones undergoes rarefaction or is replaced by a lace-like spiculated pattern beneath the periosteum; this change is best marked in the middle phalanges of the fingers (Fig. 200) but is also seen in the lower part of the neck of the femur, below the condyles of the tibiæ, in the pelvic bones and elsewhere. The terminal tufts of the distal phalanges of the fingers may show marked resorption and sometimes almost total disappearance. In one case in a girl of fifteen whose epiphyses had not closed, although all the bones of the skeleton showed advanced decalcification, the radiographs showed normal bone density in the juxtepiphyseal line of all the long bones, the vertebræ, the phalanges, and the metacarpals.



FIG 200 Osteitis fibrosa cystica The patient was a girl of 15. There is severe generalized rarefaction of the bones of the hands There is typical subperiosteal resorption of the first and second phalanges The juxtepiphyseal line near the lower epiphyses of the radius and ulna shows almost normal bone density.

Symptoms Associated with Renal Changes. *Polyuria and polydypsia are associated*



FIG 198 Long-standing case of osteitis fibrosa cystica The ribs of both sides, especially the right, have collapsed laterally.

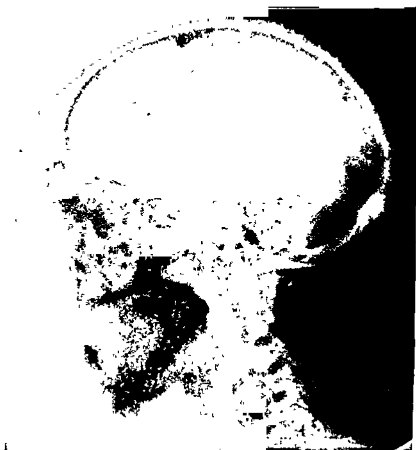


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Symptoms Associated with Renal Changes. Polyuria and polydypsia are associated

with the hypercalciuria and hypophosphaturia, as well as with the diuretic effect of the parathormone itself. The polyuria may be so marked as to simulate diabetes insipidus (Albright and Reifenstein, 1948).

The incidence of renal stones and nephrocalcinosis has been referred to. Every case of calcium-containing stone should be investigated for hyperparathyroidism and the



FIG 201 Diffuse nephrocalcinosis of both kidneys due to hyperparathyroidism.

diagnosis can only be made on biochemical grounds in the absence of skeletal changes. Three kinds of renal calculosis are associated with hyperparathyroidism. In the skeletal cases may be found soft, phosphatic stones which may form a cast of the pelvis and calyces, and which, because they lack much binding substance, may disintegrate and disappear a few weeks after the adenoma has been removed by operation. Diffuse bilateral nephrocalcinosis of the medullary and pyramidal regions of the kidney (Fig. 201),

with which small calyceal or pelvic stones may be associated, is not uncommon; in early cases this change may be limited to multiple small calcific foci around the lower calyces of both kidneys while in advanced cases it is an extensive, widely spread, calcific change. Thirdly the stone may [illegible] (Fig. 202). The calyceal stones will give rise to all the symptoms of renal calculi including



FIG 202 Massive stone in the pelvis and calyces of the right kidney. The patient had an adenoma of the parathyroid removed

colic and obstruction; the kidneys may become infected either spontaneously or following surgical removal of the stones which later tend to recur; subsequent changes will include pyelonephritis and pyonephrosis calling for nephrectomy. Thus, many of the patients have, by the time hyperparathyroidism has been diagnosed, already had multiple operations for the removal of recurrent stones or may have had one kidney removed.

Renal function is often impaired and in some cases is poor, consequent upon the calcification and slowly progressive nephrosclerosis. In a proportion of cases the urine is constantly of low specific gravity, the kidney being unable to concentrate it (hyposthenuria). Hellstrom (1950) has stressed the importance of this change in diagnosis, and has also pointed out the incidence of hypertension in late cases. After many years, if the

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per day, the estimation being done in the last 3 days of a six-day period on the diet. 125–150 mg. of urinary calcium per day is normal; 150–200 mg. per day is suspicious of hyperparathyroidism and 200 mg. or more would strongly favour such a diagnosis.

Differential Diagnosis

Skeletal Diseases. The radiographic appearances of the rarefied bones may suggest osteomalacia which does not, however, show the large cysts and the subperiosteal resorption of hyperparathyroidism; Milkman's fractures are characteristic of osteomalacia; in this condition the serum calcium is normal though the serum phosphorus may be low.

Paget's disease does not affect the entire bony skeleton; the serum calcium and serum phosphorus are normal while the alkaline phosphatase is raised.

Multiple myelomatosis may closely mimic hyperparathyroidism. In the skull the areas of rarefaction are punched out rather than granular though the rarefied zones in the long bones may be difficult to distinguish from those in hyperparathyroidism. The serum calcium is normal or elevated and the serum phosphorus is usually normal but sometimes low; the alkaline phosphatase is very rarely elevated and there may be hypercalciuria. The presence of Bence-Jones proteose in the urine is strongly suggestive of myelomatosis but the discovery of myelomatous cells in the sternal marrow puncture material is diagnostic.

Metastatic osseous carcinoma may closely mimic hyperparathyroidism, though the metastatic lesions are usually well demarcated and surrounded by normal bone. The serum calcium is commonly raised in advanced cases and there is then hypercalciuria; the serum phosphorus is usually normal though it may be raised. A primary malignant focus can usually be found in the breast, prostate, bronchus, thyroid, or kidney.

In polyostotic fibrous dysplasia there are patchy fibrous deposits in bones often having a segmental distribution, the remaining parts of the bone being normal. There are areas of cutaneous pigmentation and in females there may be sexual precocity. The serum calcium is normal while the alkaline phosphatase may be high.

The discovery in a patient of solitary bone cysts and osteoclastomata calls for a general assessment of the bony skeleton to exclude hyperparathyroidism; the serum calcium is normal in these cases.

Sarcoidosis of Boeck may occasionally mimic hyperparathyroidism since there may be hypercalcæmia, hypercalciuria, a raised alkaline phosphatase, renal stones and bone changes; the small punched-out areas of rarefaction in the phalanges differ from the changes in those bones in hyperparathyroidism. There is no generalized decalcification of the skeleton.

Renal Conditions. The nephrocalcinosis of hyperparathyroidism may be confused with that occurring in other conditions. In hypervitaminosis D there is an elevated serum calcium and impaired renal function, with microscopic and occasionally macroscopic calcification; the serum phosphorus is normal. In milk-drinker's syndrome (Burnett, Commons, Albright, and Howard, 1949) the serum calcium is high, renal function is poor, and there may be gross radiological calcification and extensive metastatic calcification beneath the skin and around joints. Nephrocalcinosis may be associated with pyelonephritis and rarely with chronic glomerulonephritis. In many cases of nephrocalcinosis no cause can be found. Hyperparathyroidism is diagnosed by the blood chemistry and the calcium balance tests.

patient is not relieved by parathyroidectomy, death may result from uræmia preceded by anuria, or from cerebro-vascular incidents dependent upon the hypertension.

Symptoms Due to Hypercalcæmia. Muscular hypotonia and general muscular weakness result from the hypercalcæmia; there is a diminution in neuro-muscular irritability which can be demonstrated by muscular electrical reactions. In the electrocardiogram there may be a shortening of the Q-T interval (Kellogg and Kerr, 1936). Crystals of calcium phosphate, demonstrable by the use of a slit-lamp, may be seen in the conjunctiva of the palpebral fissure (Walsh and Howard, 1947). Band-keratitis, consisting of calcific deposits in the periphery of the cornea, was noted by Cogan (1947).

Physical Signs. Most of the physical signs are evident from what has been described. A tumour in the neck resulting from the adenoma is only felt very occasionally; it has the character of a swelling of the thyroid gland. Nodular foci of subcutaneous calcification occur occasionally, especially round the elbow. Barium radiography of the œsophagus may reveal a filling defect resulting from the external pressure of a large adenoma.

Acute Hyperparathyroidism. This term refers to a sudden and sometimes fatal deterioration in the general condition of a patient with advanced hyperparathyroidism believed to be due to precipitation of calcium salts in the renal tubules and in other organs, possibly brought about by sudden dehydration, resulting for example from vomiting. Cases have been reported by Hanes (1939) and by Smith and Cooke (1940).

Peptic Ulcer. Ulcer of the stomach and the duodenum is not uncommonly associated with hyperparathyroidism (Rogers, 1946). Haynes (1950), examining the Mayo Clinic cases, showed that approximately a quarter of cases with proved hyperparathyroidism had active peptic ulceration or had had clear evidence of such in the past; an even higher percentage had had digestive symptoms suggestive of ulcer. The explanation for this association is not clear but it has been suggested that the hypercalcæmia in some way predisposes to ulcer formation.

Polyendocrine and Parathyroid Adenomas. Underdahl, Woolner, and Black (1953) reported 8 cases in which islet-cell tumours of the pancreas and also pituitary tumours were associated with adenomata of the parathyroid gland. No explanation has yet been offered for this association.

Biochemical Findings

In cases in which there are skeletal changes, the clinical history and the radiographic picture are complementary to the biochemical changes in making the diagnosis. In the renal group the clinician must depend entirely upon the result of biochemical tests on the blood and the urine; in fact the diagnosis is made in the laboratory.

The serum calcium is the most important finding. It has usually been taught that the normal serum calcium varies between 9·0 and 11·0 mg. per 100 c.c. of blood. It is now believed that the upper normal figure is 10·4 mg. and that levels of serum calcium above this are in keeping with a diagnosis of hyperparathyroidism which, though mild, could result in the formation of renal stones (Keating, 1955). In severe cases the serum calcium may be elevated to 13·0 or 18·0 mg., while in milder cases it may be nearer to the upper limit of normal. The serum phosphorus usually varies between 2 and 3 mg. though in a proportion of cases it remains normal. The serum alkaline phosphatase is normal in cases with renal stones but raised if skeletal changes are present. The urinary calcium should be estimated with the patient on a low-calcium diet containing 125–150 mg. of calcium

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Metastatic osseous carcinoma may closely mimic hyperparathyroidism, though the metastatic lesions are usually well demarcated and surrounded by normal bone. The serum calcium is commonly raised in advanced cases and there is then hypercalciuria; the serum phosphorus is usually normal though it may be raised. A primary malignant focus can usually be found in the breast, prostate, bronchus, thyroid, or kidney.

In polyostotic fibrous dysplasia there are patchy fibrous deposits in bones often having a segmental distribution, the remaining parts of the bone being normal. There are areas of cutaneous pigmentation and in females there may be sexual precocity. The serum calcium is normal while the alkaline phosphatase may be high.

The discovery in a patient of solitary bone cysts and osteoclastomata calls for a general assessment of the bony skeleton to exclude hyperparathyroidism; the serum calcium is normal in these cases.

Sarcoidosis of Boeck may occasionally mimic hyperparathyroidism since there may be hypercalcæmia, hypercalciuria, a raised alkaline phosphatase, renal stones and bone changes; the small punched-out areas of rarefaction in the phalanges differ from the changes in those bones in hyperparathyroidism. There is no generalized decalcification of the skeleton.

Renal Conditions. The nephrocalcinosis of hyperparathyroidism may be confused with that occurring in other conditions. In hypervitaminosis D there is an elevated serum calcium and impaired renal function, with microscopic and occasionally macroscopic calcification; the serum phosphorus is normal. In milk-drinker's syndrome (Burnett, Commons, Albright, and Howard, 1949) the serum calcium is high, renal function is poor, and there may be gross radiological calcification and extensive metastatic calcification beneath the skin and around joints. Nephrocalcinosis may be associated with pyelonephritis and rarely with chronic glomerulonephritis. In many cases of nephrocalcinosis no cause can be found. Hyperparathyroidism is diagnosed by the blood chemistry and the calcium balance tests.

Surgical Treatment

The treatment of hyperparathyroidism is the removal of the adenoma or adenomata or the subtotal resection of hyperplastic parathyroid tissue. Radiotherapy is ineffective. Without operation the patient's health slowly deteriorates though death may be delayed for many years. The milder grades of hyperparathyroidism associated with renal calculi are consistent with long years of active life.

The Operation. The removal of a large parathyroid adenoma in the neck is usually

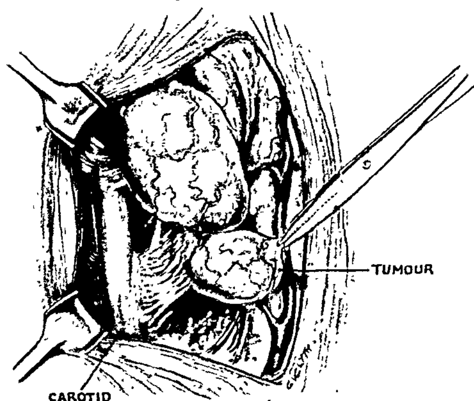


Fig 203 Operative exposure for removal of a parathyroid adenoma The thyroid gland and isthmus are shown fully mobilized. The tumour here weighed 3 gm and was situated below the right lobe of the thyroid gland.

easy but the search for the very small tumour may be prolonged, tedious, and difficult. Moreover, the presence of an occasional tumour in the mediastinum requiring mediastinotomy for its removal, introduces an element of uncertainty if the surgeon fails to find the tumour in the neck.

Anæsthesia is induced by intravenous pentothal followed by intratracheal gas and oxygen, after preliminary infiltration of the front of the neck with a local anæsthetic.

Using a Kocher's curved incision, midway between the thyroid cartilage and the manubrium sterni, the skin flaps with the platysma muscles are dissected apart and held by retractors as in the operation for the exposure of the thyroid gland. The cervical fascia is divided in the middle line from just below the hyoid bone to the upper border of the sternum and the infra-hyoid muscles are cleared from the front and the sides of the lobes of the thyroid which are then brought into view and mobilized. The inferior thyroid

arteries and veins and the recurrent laryngeal nerve, are defined. Meticulous hæmostasis is necessary throughout the operation, since staining of the tissue layers with blood may render the exposure of the normal parathyroids and of the tumour difficult or impossible. The upper and the lower parathyroid glands are then sought, first on one side and then on the other. When these have been identified, they should not be disturbed by undue dissection nor unnecessary biopsy because of the danger of damaging their blood supply especially since the glands may have undergone partial atrophy.

At any stage during the dissection, an adenoma may be encountered, the medium-sized and large ones being usually readily found (Fig. 203). It is then sufficient to dissect out the adenoma, ligature the pedicle and remove it. The surgeon must then examine the other possible sites for a second tumour.

If, however, after a preliminary inspection of the operation area, no adenoma is found, a more meticulous examination of known sites must be proceeded with including the fat below the thyroid gland in the neck and in the accessible upper part of the anterior mediastinum. The space behind the œsophagus and trachea which leads into the upper part of the posterior mediastinum and which is free from fat, should be examined by blunt dissection and then by the finger for the presence of a tumour. If these spaces on either side do not contain adenomata, further prolonged search may be necessary in the lowest part of the neck and behind the upper part of the sternum, the dissection being carried out with infinite care so as to avoid seepage of blood which would impede progress. The surgeon may mistake small yellow lobules of fat, lymphatic glands or small outlying adenomata of the thyroid, for tumours of the parathyroid, and facilities for frozen sections should be available in the theatre to enable the differentiation to be made while the surgeon continues his search. A small vascular pedicle descending from the inferior thyroid artery may occasionally lead the surgeon to an adenoma lodged behind the upper part of the manubrium sterni. In one case in the writer's series the adenoma was situated within the lower pole of the thyroid gland, its presence being recognized only after an incision into a slightly bulging lower pole of thyroid gland had revealed the yellowish-red tissue of the adenoma. In difficult cases if no tumour is found in the neck the surgeon should satisfy himself of the identity of three normal parathyroid glands before he concludes that an adenoma is present outside the neck and probably in the anterior superior mediastinum. Tumours in the mediastinum probably do not number more than a small percentage of the whole.

Primary Hyperplasia

If there is a primary hyperplasia of all four parathyroid glands, the full extent of the hyperplastic tissue should first be determined, after which three of the hyperplastic glands should be removed and a subtotal removal of the fourth gland carried out, leaving 100–200 mg. of tissue, carefully preserving the blood supply.

Mediastinotomy

If the surgeon fails to find an adenoma in the neck, in a patient in whom the diagnosis of primary hyperparathyroidism is certain, anterior mediastinotomy should be carried out at a second operation a fortnight or so later. Intra-tracheal anæsthesia is used. A curved incision is made from the centre of the cervical incision downwards to the xiphisternum. The sternum is exposed and the upper border and posterior surface of the

manubrium are defined and freed from the tissues behind it. Using a special sternum chisel, the manubrium and the body of the sternum are cut in the middle line from the suprasternal notch to the xiphoid or to just below the fourth costal cartilage; in the latter case, a transverse incision is made through the body of the sternum at that level leaving the xiphisternum intact. The divided halves of the sternum are separated and a retractor is inserted to expose the mediastinum. A search is made in the fat behind the sternum and beneath the thymic fascia, if necessary down to the pericardium. The mediastinal pleuræ, if necessary are displaced outwards. A vascular pedicle descending from the inferior thyroid artery may be a guide to the presence of the adenoma. After removal of the tumour, the two halves of sternum are approximated by catgut sutures placed through its periosteum and the overlying fascia; the subcutaneous tissues and skin are then sutured.

Post-operative Course

Biochemical Changes

Once the excess of circulating parathormone derived from the adenoma or the hyperplastic glands has been removed from the body, rapid adjustments in the calcium and phosphorus metabolism take place. The serum calcium falls to normal or sub-normal, often within 24 hours or a little longer. When extensive skeletal disease is present, the serum calcium may fall to levels as low as 7 mg. or less, consequent upon the withdrawal of calcium from the blood to the bones. The very low serum calcium figures slowly rise during the next few days, gradually returning to normal. The serum phosphorus rises gradually to normal, usually over several days. Especially in the first 24 hours but also in the following few days, there is a marked oliguria, believed to be due to the withdrawal of the diuretic effect of the circulating parathormone. The 24-hour excretion of calcium and phosphorus in the urine falls rapidly and may approach zero for the first 2 days. The alkaline phosphatase remains at a high level for weeks or months in skeletal cases until much recalcification of the skeleton has taken place (Table II).

Tetany

Symptoms of tetany usually develop within 1–3 days after removal of the adenoma though they may be mild. Tingling of the fingers and toes are always noticed and Chvostek's sign can usually be elicited. Carpopedal spasms occur only in the most advanced cases with a considerably reduced serum calcium. In cases with renal stones alone in which the serum calcium may not be so high, the symptoms of tetany are usually minimal and are limited to tingling in the fingers which may be so slight that it is not complained of by the patient. Tetany is the result of the hypocalcæmia, which in turn results from the rapid transit of calcium into the bones, the remaining atrophied parathyroid glands not being able immediately to compensate for this loss. The treatment consists of the administration of calcium gluconate by mouth or intramuscularly, depending on the severity of the tetany; if painful carpopedal spasms are present 10 c.c. of 20 per cent calcium gluconate should be given intravenously and the dose repeated if necessary. The administration of parathormone is much less effective in relieving tetany.

If all parathyroid tissue has been removed or temporarily damaged, chronic tetany results from hypoparathyroidism and this occurs occasionally in spite of careful surgery. The treatment by dihydrotachysterol (A T 10) and calcium gluconate has been referred to in an earlier paragraph.

TABLE II

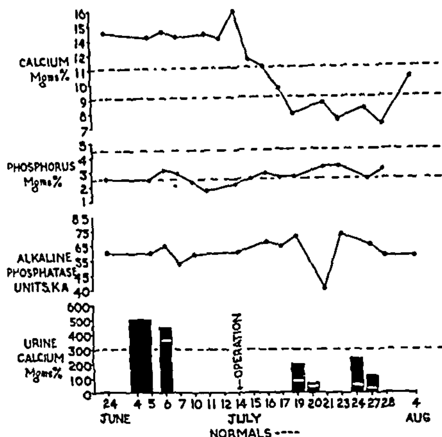


Chart showing the levels of calcium, phosphorus, and alkaline phosphatase in the blood in a case of primary hyperparathyroidism. The pre-operative urine calcium was high and was much reduced after operation. Note the fall of the serum calcium to very low levels after the tumour had been removed The phosphorus has risen post-operatively but only slowly

RENAL CALCULI

Soft, muddy deposits of calcium phosphate in the renal pelves and calyces may disappear in a few weeks following the removal of the parathyroid adenoma, with the help of copious fluids and the cautious administration of ammonium chloride to acidify the urine, thereby rendering the phosphate soluble; since the use of ammonium chloride results in an increase in the urinary excretion of calcium, it should be used only for a limited time. Compact stones, which are usually composed of calcium phosphate and calcium oxalate, require the usual surgical treatment of the idiopathic calcium-containing stone.

RECALCIFICATION OF THE SKELETON

The return to a normal bone density occurs very slowly and full doses of calcium and vitamin D are necessary for long periods in skeletal cases; periodic radiographs are desirable. Normal bone density is not usually achieved until some years after operation. Bone cysts do not necessarily disappear. Ultimately the bones regenerate and may become more dense than normal bones. There is nothing more spectacular in the whole range of surgical achievement than the rehabilitation of the worst cases of skeletal

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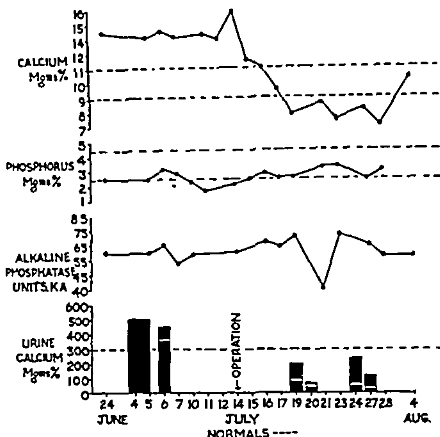


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hyperparathyroidism. The pain disappears and the crippling weakness is replaced by a return to normal activity. In the worst cases orthopædic treatment is needed for the correction of deformities.

OXYPHIL ADENOMA OF THE PARATHYROID

An adenoma consisting entirely of oxyphil cells is found occasionally. The patient presents with a mobile swelling in the region of the thyroid gland, which moves on swallowing and is usually mistaken for an adenoma of the thyroid. These rare tumours do not secrete parathormone and are therefore not associated with skeletal or renal changes. The treatment is simple surgical removal.

CARCINOMA OF THE PARATHYROID

Carcinoma of the parathyroid, producing parathormone and hence the symptoms of hyperparathyroidism, was first reported by Meyer, Rosi, and Ragins (1939) and a few other cases have been reported in the literature. Microscopically the cells resemble the adenomata but have a greater irregularity in their cell structure. Infiltration into the surrounding tissues of the neck and metastasis into the local lymph glands as well as to the lungs and the mediastinum have been reported. Surgical treatment consists of wide excision of the affected gland and of the surrounding fat.

SECONDARY HYPERPARATHYROIDISM DUE TO RENAL INSUFFICIENCY

In patients with renal insufficiency who have a severe nitrogen retention, the serum phosphorus may be elevated and there is, in fact, a phosphorus retention; such a condition may occur in patients with congenital cystic kidneys, chronic nephritis, and in advanced obstructive conditions such as urethral valves with bilateral hydronephrosis. The raised serum phosphorus tends to bring about a reduction in the serum calcium level, which in turn results in a hyperplasia of the parathyroid glands and a consequent increase in the circulating parathormone, in an effort to retain the serum calcium at normal levels. This hyperplasia is designated secondary hyperparathyroidism. In some cases subperiosteal resorption of bone may be noted radiologically and calcium phosphate may be deposited in the tissues. Apart from giving rise to diagnostic difficulties, as to whether one is dealing with primary or secondary hyperparathyroidism, this condition is not of very great surgical importance.

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These estimates, based partly on published work and partly on my own experience, indicate that in average conditions 1 blood transfusion in every 500 is likely to be followed by some undesired complication, usually hepatitis, and that between 1 in 1500 and 1 in 50,000 recipients may have their life endangered. If the transfusion is hurried or given by inexpert workers the risks are at least doubled. It therefore follows that transfusions must not be given unless, without transfusion, the likelihood of the patient dying is 1 in 1500 or more, when with transfusion death is not to be expected. For example, transfusion in all cases of severe hæmatemesis and melæna is justified because without transfusion the mortality is 25 per cent, with transfusion but 6 per cent; but it cannot be justified if it is used merely to raise the hæmoglobin level of a woman with iron deficiency anæmia just before operation for fibroids; such patients should have their anæmia treated beforehand.

BLOOD GROUPS

The ABO System

Landsteiner in 1901 showed that the red cells of humans could be divided into three classes by their reaction with the serum of other humans, and von Decastello and Sturli discovered a fourth. The classification is made clear in the Table, where + indicates that the serum indicated by the column agglutinates the cells indicated by the row.

Cell From	Serum From			
	O	A	B	AB
O	O	O	O	O
A	+	O	+	O
B	+	+	O	O
AB	+	+	+	O

It was then shown that cells from any donor could be injected into the bloodstream of any recipient provided that the serum of the recipient does not agglutinate donor cells. If the serum of the recipient does agglutinate the donor cells, there will be a more or less violent reaction inside the recipient; the cells will be lysed and the recipient may be killed. It appears that persons of group AB can receive blood from anybody, and that persons of group O can give blood to anybody; this is not quite true, but sufficiently near the truth to be applied in really grave emergencies.

The factor in the cell which confers on its specific property of being agglutinated by the appropriate serum is the agglutinogen or blood group antigen: the serum factor which agglutinates the cells is the *isohæmagglutinin* or naturally occurring (non-immune) blood group antibody, anti-A or anti-B. The concentration of antibody varies greatly; it may seem to be absent, or it may be demonstrable when the serum is diluted several hundred times. The ABO blood system is the most important of the various blood group systems, and if the patient is a female who has never been pregnant or a male and has never before been transfused, then if transfusion will be life saving it is the ABO groups compatibility which is essential.

CHAPTER XII

BLOOD TRANSFUSION

GEORGE DISCOMBE

NOBODY questions the power of blood to save lives; and blood transfusion has become one of the great life-savers of the twentieth century. Unfortunately blood transfusion can kill or injure as well as save life and it is wise before discussing its benefits, which are well known, to consider its dangers, which are often forgotten. These can be classified into three groups: the first, dangerous to life or causing prolonged ill-health; the second, alarming to the physician and uncomfortable for the patient but without risk to life or health; the third void of immediate danger, but storing up risks which can make subsequent transfusions dangerous or subsequent pregnancy unfruitful. The first two groups can be tabulated, their frequency assessed and the risk of death or serious ill-health estimated; the third group is more complex and requires more detailed study.

GROUP I—COMPLICATIONS OF TRANSFUSION ENDANGERING LIFE

A. Any Transfusion, However Carefully Performed

COMPLICATION	PROBABLE FREQUENCY	PROBABLE MORTALITY
Hepatitis	1 in 150 to 1 in 6000	10–20 per cent
Unpredictable hæmolytic reaction	1 in 10,000	25 per cent
Infected blood	1 in 500,000	50 per cent
Serologic incompatibility	Should be zero	
Total	1 in 6000 to 1 in 150	1 in 50,000 to 1 in 1500

B. Transfusion in a Hurry, Single Worker or Inexperienced Team

COMPLICATION	PROBABLE FREQUENCY	PROBABLE MORTALITY
Hepatitis	Up to 1 in 100	10–20 per cent
Infected blood	Up to 1 in 5000	50 per cent
Incompatibility	1 in 1000 or more	10 per cent
Total	Up to 1 in 95	Up to 1 in 800

GROUP II—UNCOMFORTABLE COMPLICATIONS

COMPLICATION	PROBABLE FREQUENCY	PROBABLE MORTALITY
Allergic reactions, e.g. urticaria	about 2 per cent	nil
Febrile reactions	from 1–8 per cent	nil

If cells carrying a particular antigen and suspended in saline are exposed to the action of an excess of the corresponding "albumin" or "indirect" antibody, then they can no longer be agglutinated by the "saline" antibody to that antigen. This is the "blocking" action once used to detect these antibodies.

The "Coombs" or "Anti-Globulin" test detects "albumin" or "indirect" antibody or sub-agglutinating quantities of "saline" antibody. It depends on the facts that (*a*) an antiserum to human plasma proteins free from antibodies to human red cells can be prepared in rabbits and in goats; (*b*) blood group antibodies are globulins which react with antisera to human globulin or to whole serum protein. To detect an antibody the serum suspected of containing it is allowed to react with cells of suitable antigenic type; the cells are then washed until free from serum protein (three or four washings using a saline volume 50 times the volume of the residual fluid) and then allowed to react with the antiserum to human globulin; if agglutination occurs, an antibody reacting with a red cell antigen must be present in the original serum. Proper positive and negative controls are essential: combination of antibody with cell antigen may occur *in vitro* as a deliberate part of an experiment when the test is called an "indirect" test; or *in vivo* when cells drawn from the subject are washed and tested with antiglobulin serum; this is the "direct" Coombs test.

Red cells react with some antibodies more easily if they are first treated with a proteolytic enzyme, but their capacity to react with other antibodies may be impaired. The only application of this principle which is likely to attain routine status is Löw's activated papain method, by which albumin anti-Rh sera can be made to agglutinate cells suspended in saline.

Detection of Antibodies

CROSS-MATCHING. The function of cross-matching is to discover whether the recipient of a transfusion has antibodies which will react with and destroy the cells which it is proposed to transfuse. A really complete cross-match involves tests

(*a*) In saline, to detect non-immune antibodies such as anti-A, anti-M, anti-P.

(*b*) An antiglobulin test to detect nearly all immune antibodies.

(*c*) In albumin to confirm (*b*) and to use in case a technical fault develops in (*b*).

Such a set of tests requires 3–4 hours in a very well equipped laboratory, and is only really essential with recipients who have borne children affected by hæmolytic disease of the newborn, or have had previous transfusions—the "dangerous recipients" of Dunsford and Bowley (Class A). Somewhat less dangerous as recipients are parous women who have never received transfusions, whose children were perfectly healthy at birth (Class B). Least dangerous are those who have neither been pregnant nor received a transfusion (Class C).

Normally for less dangerous and least dangerous subjects one can use tests in saline and albumin, omitting the antiglobulin tests.

EMERGENCY CROSS-MATCHING increases the risk to the patient. In the hands of the expert who is prepared to refuse to issue blood in the event of the slightest doubt, the risk may be no more than doubled, but in the hands of the inexpert junior who is being harassed by his chief the risk is increased ten or twentyfold. It is therefore obvious that any demand for blood should be made several hours—preferably a full working day—*before it is* needed. This can usually be done, but there is always the patient with a bleeding

The Rhesus Factor

The hypotheses required to explain the Rh factor are very simple provided that you are content to leave about 1 per cent of the cases unexplained; if you have to explain the last 1 per cent, the hypotheses become very complicated.

The Rhesus factor was discovered by Landsteiner and Weiner in 1940 and within a few months incriminated as a cause of transfusion accidents and as a cause of hæmolytic disease of the new-born. It appeared to be a single antigen which, when injected into persons lacking it (Rhesus negative subjects) sometimes caused the development of a specific antibody, anti-Rh, which reacts with Rh positive cells just as vigorously and with the same consequences as does anti-A with A cells and anti-B with B cells. Sensitization by injection of red cells can occur from transfusion, injection of parental blood shortly after birth (a procedure once thought to prevent and cure hæmorrhagic disease of the new-born), or injection of fœtal blood into the maternal circulation through the placenta especially during labour.

Rhesus negative subjects are readily immunized by transfusion (about two-thirds from a single transfusion) less readily by pregnancy, though of all Rh negative women who have borne children, about 1 in 7 have developed Rh antibodies. If a blood transfusion of Rh positive blood be given to someone who possesses anti-Rh, the transfused blood is rapidly destroyed, and renal failure may follow.

This is the third class of dangers due to transfusion—sensitization by pregnancy or transfusion to an antigen carried on the injected blood cells and hæmolysis of the blood of a fœtus subsequently conceived or of transfused blood which contains that antigen. The antigen concerned is usually the Rhesus antigen, but other antigens can act in the same way; of these the best known and most important are known as Kell, Duffy, S. Antibodies to these are fortunately rare—about a hundredth of the frequency of antibodies to the Rhesus factor.

Spontaneous and Immune Antibodies

Some antibodies to blood group antigens occur spontaneously; such are the common anti-A and anti-B, and the rare anti-H, anti-M, anti-N, anti-S, anti-P. These are usually cold antibodies—that is they agglutinate cells more intensely at + 4°C. than they do at room temperature or at 37°C. Immune antibodies, produced in response to the injection of cells containing a foreign antigen (e.g. B cells into an A recipient), usually react more vigorously at 37°C than at room temperature or at 4°C.

Immune antibodies usually react in greater dilution with cells suspended in a medium containing a high concentration of protein or some other macromolecular colloid (human AB serum, 20 per cent bovine albumin, gelatin, dextran, polyvinyl pyrrolidone).

Immune antibodies are of several types. The first, because most easily recognized, agglutinates cells suspended in physiological saline, and is therefore termed a "saline antibody." The second does not agglutinate cells suspended in saline, but does agglutinate cells suspended in protein-rich media such as albumin solution—it is therefore termed an "albumin antibody." The third does not agglutinate cells at all, but does attach itself to them; this antibody attached to cells will react with antiserum to human globulin, which causes the "sensitized" cells to agglutinate. This type of antibody is often referred to as "indirect" antibody, as "sensitizing" antibody or as "cryptagglutinoid."

If cells carrying a particular antigen and suspended in saline are exposed to the action of an excess of the corresponding "albumin" or "indirect" antibody, then they can no longer be agglutinated by the "saline" antibody to that antigen. This is the "blocking" action once used to detect these antibodies.

The "Coombs" or "Anti-Globulin" test detects "albumin" or "indirect" antibody or sub-agglutinating quantities of "saline" antibody. It depends on the facts that *(a)* an antiserum to human plasma proteins free from antibodies to human red cells can be prepared in rabbits and in goats; *(b)* blood group antibodies are globulins which react with antisera to human globulin or to whole serum protein. To detect an antibody the serum suspected of containing it is allowed to react with cells of suitable antigenic type; the cells are then washed until free from serum protein (three or four washings using a saline volume 50 times the volume of the residual fluid) and then allowed to react with the antiserum to human globulin; if agglutination occurs, an antibody reacting with a red cell antigen must be present in the original serum. Proper positive and negative controls are essential: combination of antibody with cell antigen may occur *in vitro* as a deliberate part of an experiment when the test is called an "indirect" test; or *in vivo* when cells drawn from the subject are washed and tested with antiglobulin serum; this is the "direct" Coombs test.

Red cells react with some antibodies more easily if they are first treated with a proteolytic enzyme, but their capacity to react with other antibodies may be impaired. The only application of this principle which is likely to attain routine status is Löw's activated papain method, by which albumin anti-Rh sera can be made to agglutinate cells suspended in saline.

Detection of Antibodies

CROSS-MATCHING. The function of cross-matching is to discover whether the recipient of a transfusion has antibodies which will react with and destroy the cells which it is proposed to transfuse. A really complete cross-match involves tests

(*a*) In saline, to detect non-immune antibodies such as anti-A, anti-M, anti-P.

(*b*) An antiglobulin test to detect nearly all immune antibodies.

(*c*) In albumin to confirm (*b*) and to use in case a technical fault develops in (*b*).

Such a set of tests requires 3–4 hours in a very well equipped laboratory, and is only really essential with recipients who have borne children affected by hæmolytic disease of the newborn, or have had previous transfusions—the "dangerous recipients" of Dunsford and Bowley (Class A). Somewhat less dangerous as recipients are parous women who have never received transfusions, whose children were perfectly healthy at birth (Class B). Least dangerous are those who have neither been pregnant nor received a transfusion (Class C).

Normally for less dangerous and least dangerous subjects one can use tests in saline and albumin, omitting the antiglobulin tests.

EMERGENCY CROSS-MATCHING increases the risk to the patient. In the hands of the expert who is prepared to refuse to issue blood in the event of the slightest doubt, the risk may be no more than doubled, but in the hands of the inexpert junior who is being harassed by his chief the risk is increased ten or twentyfold. It is therefore obvious that any demand for blood should be made several hours—preferably a full working day—before it is needed. This can usually be done, but there is always the patient with a bleeding

peptic ulcer, a serious accident, an abortion or an ectopic pregnancy for whom blood is demanded as quickly as possible. The art of using the blood bank lies in learning how to give the laboratory the longest possible warning in such cases; and the art of the hospital pathologist lies in learning how to provide quickly blood which is reasonably safe for such patients. These arts can only be acquired by logical reasoning from the known physiological indications for transfusion.

INDICATIONS FOR TRANSFUSION

A. **Anæmia.** When severe anæmia (Hb level below 7·5 Gm./100 ml. or 50 per cent) has persisted for more than a few days the myocardium begins to show the changes due to chronic oxygen starvation—the fatty degeneration recognized in severe cases at autopsy as "tabby-cat" or "thrush's breast" striation. If a heart thus damaged has suddenly to pump blood which contains more cells and is therefore more viscous, and to deal with an increased blood return, it often fails to do so and acute failure results, sometimes killing the patient with pulmonary œdema. The transfusion of blood into a patient who has severe chronic anæmia is therefore always hazardous and if possible should be avoided. If essential, it is wise to give repeated small transfusions of the packed cells from 450 ml. blood at an interval of 12–24 hours until the Hb level has been above 7·5 Gm. per 100 ml. for 3 or 4 days: the cells from 420 ml. blood will raise the Hb level by an average of 7 per cent or 1 Gm./100 ml. It is also possible to give exchange transfusions of the red cells from 3–4 bottles, of blood, removing whole blood in equal volume.

This risk of acute heart failure is enough to make one insist that patients with chronic anæmia should receive transfusions only when other methods of treatment will be ineffective. For example, patients with pernicious anæmia should be treated with cyanocobalamin, those with other megalablastoses with folic acid or other appropriate drugs; *transfusion does not supply the hæmopoietic factors needed for other cells of the body and quite often it kills the patient.* Nor should patients with iron-deficiency anæmia due, for example, to menorrhagia be transfused—at least, unless their Hb level is falling faster than 1 per cent daily—for the administration of iron orally or intravenously will normally cause a rise of 1 to 3 per cent daily: most women with menorrhagia will maintain a reasonable level (60–75 per cent) if given iron supplements by mouth (not more than 90–180 mgm. Fe daily as 3 tablets ferrous gluconate or ferrous sulphate) between the time they seek advice and the time of operation.

Transfusion is essential in *aplastic* or other forms of refractory anæmia; but these are rare and the diagnosis should only be accepted after full hæmatological investigation including marrow examination and trial of possible therapeutic agents.

It is almost specifically curative of the *hæmolytic crisis* of "Lederer's anæmia" whether this be favism or arseniuretted hydrogen poisoning; it also relieves the aplastic crisis of congenital spherocytosis (acholuric jaundice). In all these diseases the donor cells will either be not exposed to or not susceptible to the noxa which causes the hæmolytic episode; but transfusion is less valuable in the acquired hæmolytic anæmias wherein the transfused cells also are susceptible to the noxa Transfusion will usually relieve symptomatic anæmias due to infection, leukæmia, carcinoma, myelomatosis, etc., but its effect in uræmia is short lived.

B. Hæmorrhage. If hæmorrhage is slow but continued it may produce a severe anæmia, and this is best treated by transfusion, preferably of packed red cells. Acute hæmorrhage, however, produces not anæmia, but a reduction in blood volume. This is compensated for first by peripheral vasoconstriction, then by tachycardia and constriction of the larger arteries; if sufficiently severe the output from each beat of the heart barely distends the aorta so that the pulse disappears and blood flow is minimal. In such cases the blood flow to the skin and to muscles may be immeasurably small and the plasma drains out of the peripheral capillaries leaving blood containing a gross excess of cells. The peripheral vasoconstriction is mediated by nor-adrenaline and the sympathetic nervous system: these control also the sweat glands so that such patients are not only cold, but sweating.

Treatment consists in the immediate transfusion of any fluid which will remain in the blood vascular system. Delay here is dangerous and it is better to start off by injecting a litre or so of plasma, serum, or dextran so as to regain a blood volume which permits a measurable blood pressure, rather than to wait half an hour for blood. These patients need a litre or more of fluid in 10 minutes or less. If the patient is known to have been severely anæmic before the hæmorrhage, then and then only it is reasonable to give unmatched blood of compatible ABO and Rh groups (which will usually be Group O Rhesus negative) because severe hæmorrhage in an anæmic subject carries a great risk of death or blindness: *but in all cases, a sample of blood for cross-matching should be obtained before any fluid is infused.*

If really massive transfusions of several litres at a rate faster than a litre an hour are really essential, (as they are occasionally in bleeding from œsophageal varices or peptic ulcers) they must be given, but are sometimes followed by a state of incoagulability. The causes of this are not certainly known, but it is reasonable to give an occasional bottle of really fresh blood to restore labile clotting factors. Infants, and adults with cirrhosis of the liver, metabolize citrate only slowly, so precautions against citrate intoxication should be taken; after half a blood volume, calcium gluconate 1 G. to every litre of blood should be injected into a limb other than that receiving the transfusion, and repeated as necessary; and transfusion should be minimized. If these massive transfusions are essential it is also essential to arrange for surgical intervention as soon as there is a reasonable change of the patient surviving.

C. Other Reasons. Other reasons for transfusion are unusual. Transfusion during operation to cover actual loss of blood is reasonable, but can often be replaced by an infusion of plasma or dextran. It is quite wrong to give routine transfusion to all patients subjected to a major operation; it suggests that either the surgeon does not understand the function of transfusion or that his technique is unnecessarily traumatic—and even Judet's arthroplasty can usually be covered by dextran.

However, there are a few operations in which hæmorrhage, though rare, can be disastrous, and every patient subjected to such operations should at least be grouped and a sample of his serum preserved in the laboratory for rapid cross-matching: if pilot bottles are used it is not unreasonable to have a cross-matched bottle in reserve for such patients; but without pilot bottles this may lead to such a waste of blood that other patients are deprived of the blood they need. It is essential to consider, not merely the benefit of some individual patient, but also the possibility that, in affording him the best possible chance of survival, one might deprive others of those benefits.

THE TECHNIQUE OF TRANSFUSION

Transfusion can be *direct*, from vein to vein using a syringe with a two-way or three-way tap; this is simple, though laborious and likely to be complicated by clotting unless the tubing and syringe are siliconed and the donor heparinized; even so the apparatus should be irrigated at intervals with sterile 3·8 per cent sodium citrate. In some places this may be the only method practicable, but I have never seen it done in England. Usually an *indirect* method is used, in which blood is drawn from a donor into a sterile container containing anticoagulant, and after an interval injected into the recipient. Indirect transfusion can be given by drawing up blood from the container with a syringe and injecting it into the recipient or it can be given dropwise. Dropwise (drip) transfusion has become almost universal because of its flexibility, for by it one can administer blood at almost any rate from 40 ml. down to 1 ml. a minute, but it does need properly designed equipment which may be difficult to improvise. Each country or each province has its standard equipment and it is not yet possible to decide which is the best, if indeed any one is to be preferred. In general, one would prefer a method in which for collecting, storing, and administering the blood the manufacturer supplied a sterile disposable kit which is thrown away after use: such are available in many parts of the world. However, glass bottles are more safely transported and are likely to remain in use, especially if disposable plastic taking and giving sets are adopted. In any such set the essentials are (*a*) a filter to remove small clots, (*b*) a chamber in which the blood can be seen dripping through; (*c*) a giving needle; (*d*) an adjustable clip to control the rate of flow; (*e*) an air inlet. Some examples are shown in the Figure.

Anticoagulants. The usual anticoagulant is the acid citrate dextrose mixture of Loutit and Mollison (3 gm. anhydrous dextrose and *either* 2 gm. dosodium hydrogen citrate monohydrate, *or* 1·54 gm. trisodium citrate dihydrate + 0·55 gm. citric acid monohydrate, made up to 120 ml. with pyrogen-free water), which permits blood to be stored at 2–6 °C for 3 or 4 weeks; but disodium sequestrene (Versene, N:N:N′:N′-ethylenediaminetetraacetic acid disodium salt) used with siliconed glass and metal or with plastic containers enables platelets to survive for 24–36 hours and has other advantages. Simple citrate can be used if the blood is to be used within a few days, but is quite unsuitable for blood banks because its neutral reaction and the absence of glucose permit storage for no more than 7 days. Defibrinated blood has been used and is quite suitable for immediate transfusion.

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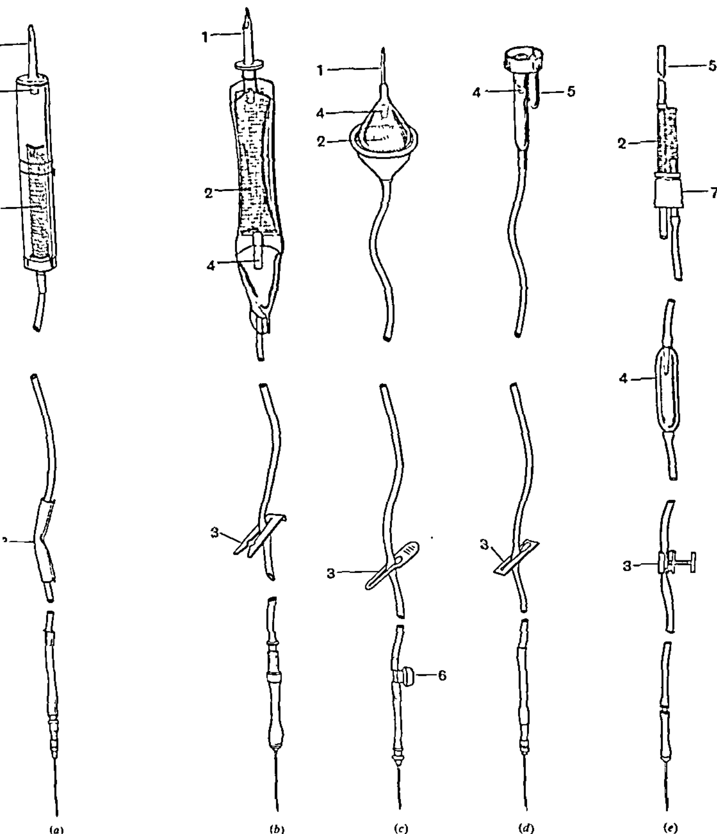


FIG 204 Different types of apparatus for administering intravenous fluids (*a*), (*b*) American sets for blood, (*c*) Danish set for blood, (*d*) American set for saline, (*e*) Original British set

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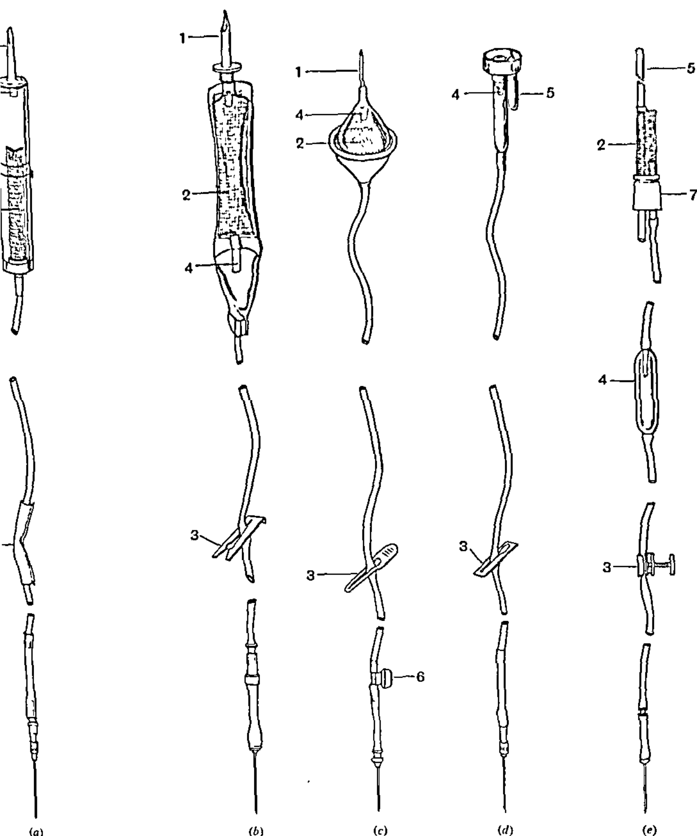


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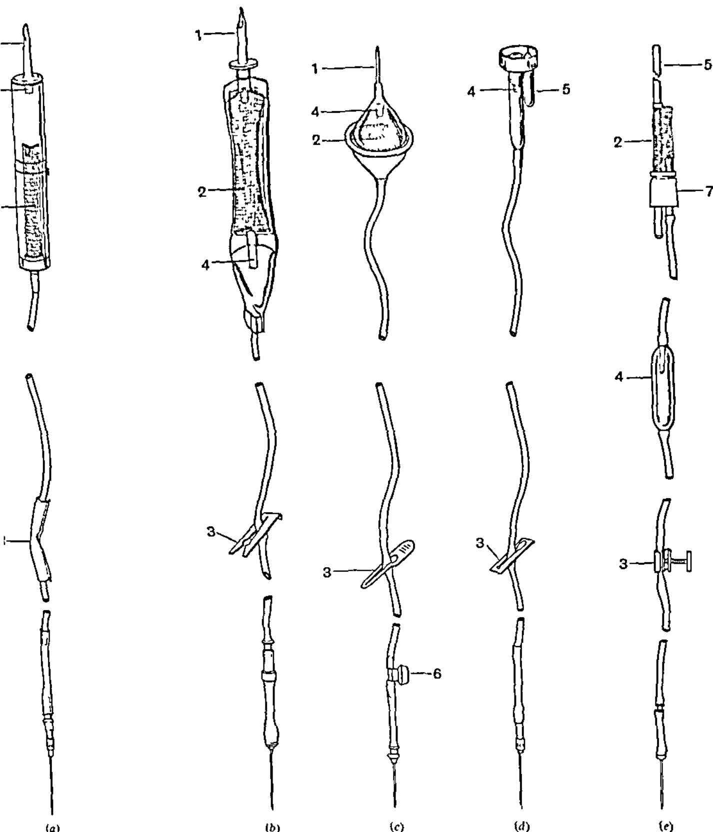


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surprising casualness, because the interval between collection and administration was so short that bacteria could not multiply: almost any container which has been boiled can be used to hold blood, but the citrate solution should be obtained from sterile ampoules or prepared extempore, boiled and used immediately, because many bacteria grow quite well in ordinary solutions of citrate or even of saline and can generate pyrogens in distilled water in a few hours. The most convenient container is a quart jug made of metal or glass, from the bottom of which blood is sucked up into a syringe through a rubber tube with a weighted end, and after turning the two-way tap on the end of the syringe, ejected through a second tube and intravenous needle into the recipient's vein. It is best to have a three-way tap on the syringe, the third nozzle being connected to a tube passing into a reservoir of isotonic sodium citrate with which the syringe and tubes can be rinsed through. An improvised gravity transfusion can be given if the container has fitted at its lower point a spout to which can be connected a rubber tube, e.g. a douche can.

Technique of Administration. The transfusionist's nightmare is first finding a vein to enter, and second, thrombophlebitis—which is rare for infusions lasting less than 8 hours but very common for those lasting 24 hours or more. The best way of avoiding thrombophlebitis is to make sure that all the fluid needed for a 24-hour period is given during an 8 hour period; but this may be impossible, when one should select three veins and change from one to the next at intervals of 6 or 8 hours. Cannulæ should not be tied into a vein unless it is essential, for cannulation, especially of the saphenous vein at the ankle, favours thrombophlebitis. If cannulation is essential, the addition of hydrocortisone free alcohol to all infusion fluids except blood (1–5 μG/ml., total dose less than 2 mgm. per hour) is said to minimize thrombophlebitis.

For ordinary work a No. 1 serum needle (S.W.G. 20) is quite large enough, but larger needles S.W.G. 18 or 15 should be used if there is any probability that high rates of flow will be needed. Insertion into veins at the limb flexures should be avoided and in all cases the needle and adjacent tubing should be firmly attached to the limb by adhesive strapping or bandages, though these must not occlude the veins feeding the vein which has been entered. If veins are difficult to find and the patient's condition is not desperate, large venous channels usually appear when a limb is wrapped in a thermostatically controlled electric blanket for 15–20 minutes, and this procedure reduces the frequency of venous spasm which occasionally appears when cold blood is run into a contracted peripheral vein. It should rarely be necessary to cut down on a vein. If you warm the limb into which the transfusion is running you increase the blood flow through the limb and hence dilute the transfused blood more rapidly; since thrombophlebitis is thought to be caused by extractives from rubber tubing, it should be minimized by warming the limb. However, vasodilatation in one limb is usually accompanied by peripheral vasodilatation elsewhere, so that warming a limb of a severely oligæmic patient may cause a further fall of blood pressure—a danger to be guarded against and if necessary overcome by rapid infusion of the first 500 ml. of blood, plasma, or plasma substitute. It is much easier to enter veins on the upper limb, and the hydrostatic pressure in the vein of the arm is lower than that in the leg, so that dilution occurs rapidly, and pooling of blood is avoided. Transfusions given into arms are rarely followed by such severe thrombophlebitis, local infection or ulceration as is often seen following transfusions into the leg.

It is sometimes desirable to force blood into the patient's circulation faster than it will run under gravity. It is unwise to do this by using compressed air, for an obstruction may

be overcome or venous spasm suddenly relax, whereupon the blood suddenly flows in, followed by most of the air to kill the patient by air embolism. It is better to use a mechanical pump such as that of Keating (*British Medical Journal* 1953, i, 94) made by the Bax Engineering Co., Wheatley, Oxfordshire, or Martin (*Lancet*, 1954, ii, 1002) made by Allen and Hanbury's, London, which can be clamped to a bedpost or held in the hand. Other pumps, some electrically driven, have been used, but those mentioned above seem simplest.

Special Types of Transfusion

(*a*) Packed cell transfusion.
(*b*) Platelet transfusion.
(*c*) Arterial transfusion.

(*a*) **Concentrated Red Cell Suspensions.** These can be extemporized from bank blood which has stood overnight by aspirating off the supernatant plasma *secundum artem* just before use. In my own laboratory we thrust an 8 in. needle through the rubber seal, but if this is not available and it is known that the blood will be used at once, it may be justifiable to remove the cap and suck off the plasma by a needle attached to a rubber tube—but this method always contaminates the blood with a few bacteria and may only be used when clinician and laboratory have complete mutual trust.

(*b*) **Platelets.** Platelets can be maintained intact in shed blood for some hours provided the blood does not contact a water-wettable surface. Few modern plastics are water-wettable, and a layer of a suitable silicone on glass and metal will render that non-water-wettable, so that if a siliconized collecting bottle and needles are used with plastic giving and taking sets, platelets can be transfused. The A.C.D. anticoagulant may be used, or 0·9 Gm. disodium N:N:N':N':ethylene diamine tetra acetate (sequestrene, versene, sodium diedetate B.P.C.) dissolved in 50–100 ml. saline for 500 ml. blood.

(*c*) **Intra-arterial Transfusion.** (Note contributed by Irvine B. Smith, F.R.C.S., Surgical Tutor, Department of Surgery, University of Leeds). It is already 75 years since Halstead (1883) successfully transfused saline, donor's blood, and the patient's own blood into the radial arteries of 3 patients suffering respectively from hæmorrhagic shock, toxic collapse, and coal-gas poisoning. But the technique lay dormant till the late war.

Intra-arterial transfusion (I.A.T.) has been thought superior to intra-venous transfusion (I.V.T.) for two reasons: that it is more beneficial to the coronary circulation and peripheral pressure; and that the rate of transfusion is faster. Experiments by Veal *et al.* (1952) on dogs have shown conclusively that in very severe oligæmic shock I.A.T. improves the systemic and coronary blood pressure more quickly, more effectively and with less blood than I.V.T.; and comparisons of the survival rates of dogs bled virtually to death and then transfused are even more favourable for I.A.T. (Kohlsteadt and Page 1943). However these advantages of I.A.T. were apparent only when treating *very severe* shock; less severe degrees responded satisfactorily to I.V.T. In clinical practice a similar superiority for I.A.T. has been claimed convincingly in several large and independent series (Porter, Sanders and Lockwood 1948, Bingham 1952).

The speed of transfusion depends on the size of the needle, the pressure applied to the blood and the zeal of the operator, which tends to be greater for I.A.T. than I.V.T. But when these factors are made equal for each method, blood can in fact be made to enter

surprising casualness, because the interval between collection and administration was so short that bacteria could not multiply: almost any container which has been boiled can be used to hold blood, but the citrate solution should be obtained from sterile ampoules or prepared extempore, boiled and used immediately, because many bacteria grow quite well in ordinary solutions of citrate or even of saline and can generate pyrogens in distilled water in a few hours. The most convenient container is a quart jug made of metal or glass, from the bottom of which blood is sucked up into a syringe through a rubber tube with a weighted end, and after turning the two-way tap on the end of the syringe, ejected through a second tube and intravenous needle into the recipient's vein. It is best to have a three-way tap on the syringe, the third nozzle being connected to a tube passing into a reservoir of isotonic sodium citrate with which the syringe and tubes can be rinsed through. An improvised gravity transfusion can be given if the container has fitted at its lower point a spout to which can be connected a rubber tube, e.g. a douche can.

Technique of Administration. The transfusionist's nightmare is first finding a vein to enter, and second, thrombophlebitis—which is rare for infusions lasting less than 8 hours but very common for those lasting 24 hours or more. The best way of avoiding thrombophlebitis is to make sure that all the fluid needed for a 24-hour period is given during an 8 hour period; but this may be impossible, when one should select three veins and change from one to the next at intervals of 6 or 8 hours. Cannulæ should not be tied into a vein unless it is essential, for cannulation, especially of the saphenous vein at the ankle, favours thrombophlebitis. If cannulation is essential, the addition of hydrocortisone free alcohol to all infusion fluids except blood (1–5 μG/ml., total dose less than 2 mgm. per hour) is said to minimize thrombophlebitis.

For ordinary work a No. 1 serum needle (S.W.G. 20) is quite large enough, but larger needles S.W.G. 18 or 15 should be used if there is any probability that high rates of flow will be needed. Insertion into veins at the limb flexures should be avoided and in all cases the needle and adjacent tubing should be firmly attached to the limb by adhesive strapping or bandages, though these must not occlude the veins feeding the vein which has been entered. If veins are difficult to find and the patient's condition is not desperate, large venous channels usually appear when a limb is wrapped in a thermostatically controlled electric blanket for 15–20 minutes, and this procedure reduces the frequency of venous spasm which occasionally appears when cold blood is run into a contracted peripheral vein. It should rarely be necessary to cut down on a vein. If you warm the limb into which the transfusion is running you increase the blood flow through the limb and hence dilute the transfused blood more rapidly; since thrombophlebitis is thought to be caused by extractives from rubber tubing, it should be minimized by warming the limb. However, vasodilatation in one limb is usually accompanied by peripheral vasodilatation elsewhere, so that warming a limb of a severely oligæmic patient may cause a further fall of blood pressure—a danger to be guarded against and if necessary overcome by rapid infusion of the first 500 ml. of blood, plasma, or plasma substitute. It is much easier to enter veins on the upper limb, and the hydrostatic pressure in the vein of the arm is lower than that in the leg, so that dilution occurs rapidly, and pooling of blood is avoided. Transfusions given into arms are rarely followed by such severe thrombophlebitis, local infection or ulceration as is often seen following transfusions into the leg.

It is sometimes desirable to force blood into the patient's circulation faster than it will run under gravity. It is unwise to do this by using compressed air, for an obstruction may

be overcome or venous spasm suddenly relax, whereupon the blood suddenly flows in, followed by most of the air to kill the patient by air embolism. It is better to use a mechanical pump such as that of Keating (*British Medical Journal* 1953, i, 94) made by the Bax Engineering Co., Wheatley, Oxfordshire, or Martin (*Lancet*, 1954, ii, 1002) made by Allen and Hanbury's, London, which can be clamped to a bedpost or held in the hand. Other pumps, some electrically driven, have been used, but those mentioned above seem simplest.

Special Types of Transfusion

(*a*) Packed cell transfusion.
(*b*) Platelet transfusion.
(*c*) Arterial transfusion.

(*a*) **Concentrated Red Cell Suspensions.** These can be extemporized from bank blood which has stood overnight by aspirating off the supernatant plasma *secundum artem* just before use. In my own laboratory we thrust an 8 in. needle through the rubber seal, but if this is not available and it is known that the blood will be used at once, it may be justifiable to remove the cap and suck off the plasma by a needle attached to a rubber tube—but this method always contaminates the blood with a few bacteria and may only be used when clinician and laboratory have complete mutual trust.

(*b*) **Platelets.** Platelets can be maintained intact in shed blood for some hours provided the blood does not contact a water-wettable surface. Few modern plastics are water-wettable, and a layer of a suitable silicone on glass and metal will render that non-water-wettable, so that if a siliconized collecting bottle and needles are used with plastic giving and taking sets, platelets can be transfused. The A.C.D. anticoagulant may be used, or 0·9 Gm. disodium N:N:N′:N′:ethylene diamine tetra acetate (sequestrene, versene, sodium diedetate B.P.C.) dissolved in 50–100 ml. saline for 500 ml. blood.

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through a vein as quickly as through an artery of equal size. However, whilst rapid I.A.T. does improve the coronary flow and oxygenation of the heart, too rapid I.V.T. of anoxic blood can precipitate heart failure and therefore may occasionally be contra-indicated.

Technique of Intra-arterial Transfusion. Amongst peripheral arteries the iliac, femoral, dorsalis pedis, brachial, radial and common carotid have all been used, cannulæ being inserted into the distal but preferably only needles into the more proximal vessels. The great danger of centrifugal transfusion has long been known and blood should always enter *towards the heart*. However, even then serious peripheral ischæmia may still follow distal ligation, thrombosis or arterial spasm caused by injury, manipulation or too rapid transfusion of cold blood. Spasm may also seriously impede the actual transfusion.

The aortic route was first used in order to remedy serious hæmorrhage when the aorta happened to be exposed at thoracotomy, but the translumbar needle has proved equally effective in making numerous other patients fit for operation (Haxton 1952, 1953). With the patient lying prone or on his right, a needle of 7 in. or longer (depending on obesity) is inserted 4 in. to the left of the 3rd lumbar spine, pushed anteromedially between the transverse processes till it meets the side of the vertebral body, and then edged forwards till a vigorous pulsating flow indicates entry to the aorta.

Certain apparatus is essential: the bellows of a sphygmomanometer or Higginson's syringe; pressure-resistant connexions such as bayonet-fitting needles, screw-capped blood bottles and stout rubber tubing whipped in place; a manometer connected by a Y tube is also needed for recording input pressure. The size of the needle is the most important single factor influencing rate of flow, and 17 S.W.G. is desirable. The danger of air embolus can be diminished very simply by connecting the bottles of blood in series between the source of pressure and the patient, but its prevention always remains the responsibility of whoever applies pressure to the blood. Such pressure is best supplied, kept constant or easily controlled from an oxygen cylinder instead of by hand bellows. A sealed unit containing suitable needles and prepared connexions, towelling and local anaesthetic, etc., should be kept sterile and readily available in the operating theatres.

Dangers. The rapid infusion of large quantities of old citrated blood may increase the probability of cardiac arrest by raising the potassium (due to damaged red blood corpuscles) or lowering the calcium (excess citrates) in the serum (*Lancet*, editorial 1954). If hæmorrhage necessitated the intra-arterial transfusion, it may increase alarmingly because of the rapid rise of blood pressure, or because the arteries are flooded with citrated blood. A large transfusion needle may cause ischæmia distal to the point of entering a peripheral artery, or concealed hæmorrhage from an aortic puncture wound.

Indications. These are probably few. The most useful application of I.A.T. is for massive unexpected hæmorrhage during thoracotomy or laparotomy when the aorta is accessible for direct puncture under visual control. Occasionally patients are seen in really urgent need of operation for hæmorrhage, injury or perforation of a viscus, but quite unfit for it because of profound shock; such patients may possibly be improved more rapidly, more effectively, with less blood and probably more safely by using intra-arterial instead of intravenous transfusion.

BLOOD TRANSFUSION ACCIDENTS

How Administrative Errors Occur

Most transfusion accidents are due to carelessness, and this may occur in the wards as readily as in the laboratory. The chief occasions for carelessness are:

(*a*) In identifying the patient.

(*b*) In labelling the specimen.

(*c*) In failing to read labels.

Confusion between two patients of similar or identical names can be prevented by using a unit record number on all request papers or by specifying the date of birth as well as the name. This is particularly important in countries where the population share only a few surnames, as in Wales or China

Errors of labelling occur most commonly if, after the specimen has been collected, it is taken to the office desk to be labelled; it may there be confused with another specimen. The empty container should be labelled, taken to the bedside, and there filled.

Many people assume that someone else has made sure that the blood offered is the correct blood for that patient. It often is not, and to avoid accidents, blood should be checked in the same way as are dangerous drugs.

In any hospital some standard procedure must therefore be adopted. Usually a special form with spaces for names, sex, age, ward, unit record number, or date of birth as well as present diagnosis, and past obstetric and transfusion history should accompany each request to the laboratory, and the information supplied thereon will decide the complexity of the cross-matching tests. The blood, once cross-matched, should bear a label which is clear and not easily defaced or removed; the best are a paper label secured by adhesive transparent tape or a label of zinc oxide strapping written on with a ball-point pen or indelible pencil. Each should carry the patient's name and unit record number (or date of birth), ward, an indication that it has been cross-matched and by whom and the date of issue. A tie-on label may be used but is not so safe. Most laboratories also insist on an issue book, in which details of each bottle are recorded at issue, and which must be signed by the person issuing the blood and the person taking it away.

Blood Transfusion Reactions

Blood may disturb the recipient's body because it is serologically incompatible, because it contains an allergen to which the recipient is sensitive, because the patient is frightened, because the blood was infected, or for no apparent reason.

Allergic reactions and those due to fear are best prevented by administering a sedative antihistamine drug parenterally just before, or orally an hour before transfusion. Promethazine hydrochloride, 25 mg., gives very good results and also seems to minimize febrile reactions.

BACTERIAL CONTAMINATION OF TRANSFUSED BLOOD. Blood grossly contaminated with living bacteria sends the patient straight into irreversible hypotensive shock. Such blood usually has the characteristic smell of rotten eggs. The prognosis is hopeless.

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(*b*) Increase in serum bilirubin and sometimes clinical jaundice.

If the recipient has a fairly low titre hæmagglutinin, it may all be adsorbed on to the cells of the transfused blood which will then persist in the recipient's circulation until an immune response develops. As newly formed hæmagglutinin increases, so the incompatible blood is destroyed, and it often happens that the cells are eliminated slowly for 2 days, then on the third day suddenly all incompatible cells disappear, clinical jaundice develops, and subsequently the hæmagglutinin titre rises rapidly to a maximum about the tenth day, thereafter declining slowly over weeks, months, or years. A hæmolysin also may appear and persist. Immune responses of this type may be delayed even longer, for I have seen an anti-S develop and cause a hæmolytic reaction after 13 days.

Clinical Manifestations. There are two modes of onset. *The first*, dramatic and of serious import, consists of pain in the loins, followed by loss of consciousness and convulsions, incontinence of fæces and hypotension: it usually occurs after quite small volumes have been administered and resembles an anaphylactic reaction. Treatment has not yet been standardized, but a nor-adrenalin drip seems reasonable, and compatible blood may be useful; however, a few patients react like this in the absence of significant serologic incompatibility, and further transfusion of these is hazardous. *The second*, usually insidious mode of onset, may include pain in the loin, usually fever, sometimes a shivering attack, sometimes hæmoglobinuria, and occasionally clinical jaundice, though an increase in serum bilirubin can always be demonstrated. Oliguria and anuria may follow, in probably less than 10 per cent of cases who have not pre-existing gross damage to their kidneys. Treatment of this type of reaction is unnecessary, unless oliguria develops, when the Borst-Bull regime should at once be adopted. In this the water intake is restricted to enough to balance insensible loss plus excretion plus vomit; about 300 g. glucose or other carbohydrate are added, giving 1200 cal., and 100 g. edible oil emulsified therein (900 cal.) the unpalatable mixture being given through a fine stomach tube; if diarrhœa develops the oil should be omitted, or 20–40 per cent glucose given through a polythene catheter inserted into the vena cava until the urinary output approaches normal. The object of these manœuvres is to provide a high calorie nitrogen-free diet to minimize endogenous and exogenous protein metabolism and the accumulation of noxious metabolites: by its aid the mortality of incompatible transfusion should be kept to about 1 per cent.

Investigation of Suspected Transfusion Accident

To investigate a suspected hæmolytic reaction one therefore needs

(i) pre-transfusion serum, which should have been stored frozen solid or at least chilled to freezing point: pre-transfusion cells are desirable but rarely available.

(ii) Post-transfusion serum and cells.

(iii) The blood bottle from which the transfusion was given. This should be capped and hurried to the laboratory for test.

Procedure

A. *Bacteriological Study.* Using 4 tubes of 20 ml. glucose agar, pour plates containing ½ and 1 ml. of the well-mixed blood. Incubate one pair of plates at room temperature for 5 days and one pair at 37° for 48 hours, examining each morning. Count the colonies which develop. A count of less than 50 per ml. (usually *Staphylococcus albus*) is usually due to chance contamination since the transfusion was started; one of over 500 ml.

(especially of coliforms) suggests that either contamination is of fairly long standing or that the bottle has been kept warm for several hours since it was contaminated.

B. *Confirmation of the ABO and Rh Type of the Transfused (Donor) Blood Cells.* This should be set up in duplicate in tubes, preferably using two different samples each of anti-A, anti-B, and anti-D serum, and the ABO grouping checked with serum from a group O subject. In practice, a tile test for the ABO group usually gives the correct answer much more quickly, but this must be checked by tests in tubes.

Special attention must be paid to the possibility of the donor blood belonging to one of the sub-groups of A; it is quite common for the A_2 of an A_2B blood to be missed, and the blood, classed as B, to be offered for a B recipient.

C. *Confirmation of the ABO and Rh type of the recipient*, using pre-transfusion cells if available, otherwise post-transfusion cells. The reactions with post-transfusion cells must be studied microscopically to discover whether all, or only some of the cells are agglutinated.

D. *Back-check on pre- and post-transfusion serum of recipient and on plasma of donor blood* using known A and B cells to confirm the ABO group.

E. *Repeat the cross-matching test* in saline and albumin, using pre- and post-transfusion serum.

F. *Set up Anti-globulin Tests.* (*a*) A direct test on pre- and post-transfusion recipient's cells. This indicates whether there are, in the recipient's circulation, foreign cells which have adsorbed antibody.

(*b*) An indirect test using donor cells and pre- and post-transfusion serum. This seeks evidence of any antibody to the donor cells.

If there is any ABO incompatibility it should appear as soon as the tile tests in B and C are performed. Rh incompatibility may be suspected from B and C and confirmed by the albumin test in E and the antiglobulin tests in F. Irregular antibodies such as anti-Kell or anti-Duffy are discovered by F(*b*); anti-M, anti-N, anti-P by the saline test under E.

Technique of Blood Grouping and Matching. On every occasion the technique adopted must be appropriate to the skill of the technician and the complexity of the problem. If there is any choice between two methods, the simpler should always be adopted. Here, only recognized standard methods are described.

Blood grouping in tubes is fairly slow since the tubes must be stood 1–2 hours before reading: but it is very reliable, especially when performed in duplicate, and very convenient when many tests are to be done. If several tests are being done, either labelling must be meticulous, or special blocks or racks to hold the tubes should be obtained and correctly oriented, e.g. marked Front and Back. Errors occur only by confusion, or when tubes are dirty, e.g. contain acid which causes false agglutination, or "teepol" or similar detergent which inhibits agglutination.

Normal Procedure. A 5 per cent suspension (approximate) of cells is made (this is best gauged by measuring 0·1 ml. normal blood into 1 ml. saline) spun down, and resuspended in saline to the original volume.

Into a tube is placed enough serum to cover the curved bottom completely (1, 2, 3 or more drops from a Pasteur pipette, or 0·1–0·5 ml. from a graduated pipette) and an equal

Macroscopic examination is performed by examining the pattern of the cell sediment, most conveniently reflected in the concave mirror of a microscope. A small, dense, even button of cells at the centre indicates no agglutination, whereas an irregular dense margin, surrounding an uneven and rather diffuse deposit of cells indicates agglutination. The sediment may be shaken up and the persistence of agglutinates noted.

Microscopical examination involves removal of part of the deposit which is spread out

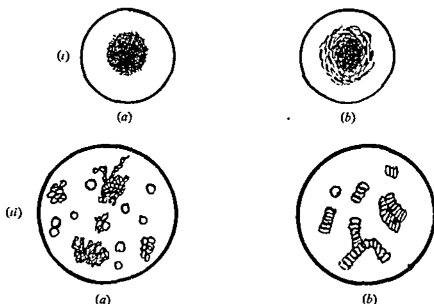


FIG 205 (i) Reactions in tubes viewed in a concave mirror
(*a*) No agglutination (*b*) Weak agglutination
(ii) Microscopical fields
(*a*) Agglutination (*b*) Rouleaux

on a slide, and examined under the $\frac{2}{3}$ in. and $\frac{1}{6}$ in. objective. Special care to differentiate agglutination from rouleau formation is needed.

ABO antibodies are easily detected by this method at room temperature: so are most antibodies to M, N, P; conversely, using known sera, the antigens A, B, M, N, P can be detected.

Cold agglutinins are most active at 4° but may interfere at room temperature on cold days. They are usually non-specific, but anti-M and anti-P are fairly common.

Rhesus antibodies can only sometimes be detected by this procedure. For these it is better to proceed as above but after 2 hours to remove the supernatant very gently and *without disturbing the sediment and replace the supernatant with an equal quantity* of 20 per cent bovine albumin, then incubate a further 15 minutes and examine microscopically. This "albumin replacement method" is particularly useful if dextran has been administered or if the patient has abnormal serum proteins causing pseudo-agglutination as in myelomatosis

ABO Blood Grouping. Cells suspended in saline; standard sera anti-A and anti-B; O serum containing anti-A and anti-B is a useful check. Incubation at room temperature (22°). Reverse check with standard A and B cells with patient's serum is desirable.

Rh Blood Typing. Cells suspended in 20 per cent bovine albumin or albumin replacement method to be used, standard serum anti-D or anti-Rh_0 Incubation at 37°.

Cross-matching. Recipient's serum, donor cells. Test to be set up in duplicate, one set at room temperature, the other at 37°; that incubated at 37° to be subjected to the albumin replacement procedure. If a hæmolysin is present most of the cells will be lysed and those which survive will be inagglutinable; but hæmolysins usually act only at 37° and require complement for their action: the complement of human serum will be destroyed by exposure to 56° for 10 or 15 minutes.

Controls must be set up; for AB grouping they should consist of known O, A, and B cells; for Rh typing known Rh positive and Rh negative cells, and in the cross-match the recipient's serum is replaced by saline. If blood is wanted very quickly it is permissible after 15 minutes to centrifuge the test for 1 minute at 1000 rev./min. and examine the deposit microscopically; any clumping is a positive reaction but false positives can be

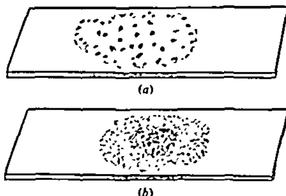


FIG 206 (*a*) Agglutination. (*b*) No agglutination; slight granularity due to evaporation

obtained easily by over-centrifugation. The method is therefore in England considered less reliable than the standard 2-hour method, but is the standard procedure in America. It is particularly reliable when technicians frequently change.

Dangers. If serum be contaminated by certain bacteria it agglutinates all cells exposed to it irrespective of their blood group. If cell suspensions be contaminated by certain other bacteria they are agglutinated by any undiluted serum, even their own. Grouping sera should therefore be dispensed in small volumes and kept in a refrigerator or frozen solid in an ice-cream conservator. Dried (lyophilised) grouping serum is available for use in the tropics. Cells of known antigenic structure can now be preserved by freezing in dilute glycerol and subsequent thawing and washing.

Slide Tests. The principle of these is that if the cell-serum mixture is spread out in a thin layer, and mixed slowly or at intervals, then agglutination occurs much more quickly. Slide tests usually work quite well with saline antibodies, but are much less satisfactory for albumin antibodies or with cells suspended in macro-molecular colloids. Slide tests are satisfactory for ABO grouping and may be useful in checking the ABO compatibility of blood, though it must be remembered that most immune antibodies including those to the Rh antigens will not be detected. Procedure: 3–4 drops serum already diluted with an equal volume of saline are spread out over an area of slide ¾ × 1 in.; 1–2 drops cell suspension or a loopful of fresh blood taken from finger or ear are added, so that the mixture is pink and translucent, not red or opaque. The slide is tilted so that the drop moves round the periphery of the spread area for one or two revolutions, then stood half a minute, then mixed again and so on. For ABO grouping a positive reaction is a

clumping into 5–10 large lumps within 2 minutes. Occasionally A_2 cells in which the blood group factor resembles A but is less active, show only granularity after 2 minutes; the slide is then placed in a wet chamber for 5 minutes and then mixed again, when A_2 cells will show 20–50 tiny clumps. Patients with antigen A_2, especially those of group A_2B, often have the antibody α_1 which reacts with A_1 but not with A_2 cells; they must therefore be cross-matched very carefully and if there is the slightest doubt A_2 recipients should receive O blood and A_2B recipients receive B blood.

Cross-matching on a slide is unreliable. In expert hands it will detect many antibodies—anti-AB, anti-D, anti-c, anti-P and some others, but the less expert will miss many of them. It should be regarded as a quick method of checking the ABO incompatibility of blood, not as a method suitable for routine use. It is particularly useful for ABO testing because the answer can be read within a few minutes and it is not affected by hæmolysins (which can destroy most of the cells in a tube cross-match at 37° and render inagglutinable those which remain). Unfortunately it also picks out non-specific cold agglutinins of quite low titre, which may confuse the less expert. If one must cross-match on a slide, one should use 4 drops of undiluted serum and a small drop or even a loopful of cell suspension, and keep in a wet chamber for at least 5 minutes; alternatively a large drop of cells suspended in albumin may be used. If any granularity appears after 5 minutes at room temperature, the wet chamber should be warmed in the 37° incubator for 5 minutes, when, if the granularity is due to cold agglutinins it will disappear, to re-appear slowly as the slide cools on the stage of the microscope.

THE ANTI-GLOBULIN TEST

Procedure. Incubate donor cells (5 per cent suspension) with an equal volume of recipient's serum. At the same time set up (*a*) a negative control consisting of washed red cells suspended in their own serum; (*b*) a positive control in which Rh positive cells are sensitized by a powerful albumin Rh antibody and (*c*) a positive control in which Rh positive cells are sensitized by a very weak albumin Rh antibody. After 1 or preferably 2 hours, wash three times with at least 50 volumes of saline, being careful to wash down the walls of the tube each time, and do not centrifuge faster than 1500 rev. per minute or longer than 2 minutes at a time. Resuspend the cells in a little saline to form a 10–20 per cent suspension.

Dilute the anti-globulin serum as recommended in the instructions—usually 1 in 40 to 1 in 64; if the optimal dilution is not known, prepare a series of doubling dilutions from 1 in 4 to 1 in 128.

On a slide place 3 or 4 drops of dilute antiglobulin serum and add 1 drop of the red cell suspension; spread over an area about 1 × 1½ in. and mix for half a minute by gentle rotation. Set by for half a minute and rotate again. Repeat for a total of 3 minutes. Compare the unknown with the positive and negative controls; it is rarely necessary to use a microscope.

If dilutions of anti-globulin serum are used, the most concentrated will agglutinate the test and all controls because there remains some trace of anti-human antibody or because cold agglutinins are present. As dilution increases, the negative and positive controls become more easily differentiated, and the correct dilution is that in which the negative control shows no clumping at all and the positive controls are both clearly positive, but one is much more tightly agglutinated than the other.

It is essential that all glassware used in this test should be scrupulously clean. Pasteur pipettes should be freshly drawn, graduated pipettes should be cleaned in chromic acid, thoroughly washed, dried, plugged, and sterilized in copper sterilizing boxes used to contain no other pipettes: tubes should be chromic acid washed. A new container of saline should be opened for each batch of work. This is because the slightest trace of human serum will inactivate the anti-globulin serum and produce false negatives.

Addendum

Subgroups of the Rhesus Factor. A few rare sera enable one to break up the crude Rhesus positive and Rhesus negative classes into smaller classes. These sera are called

anti-C or anti-rh′ anti-c or anti-hr′
anti-E or anti-rh″ anti-e or anti-hr″
anti-f or anti-hr.

With very rare exceptions, every blood sample reacts with one or both of anti-C and anti-c and with one or both of anti-E and anti-e. In this way a series of sub-groups have been defined of which the commonest are shown in the table. Antibodies can be formed only in those subjects who lack the corresponding antigen, e.g. anti-C only in those whose cells do not react with anti-C.

Label	Reaction with Anti-					Frequency (per cent)
	C	D	E	c	e	
Rh_1rh .	+	+	O	+	+	34 9
Rh_1Rh_1	+	+	O	O	+	18·5
Rh_2rh .	O	+	+	+	+	11·7
Rh_2Rh_2 .	O	+	+	+	O	2 2
Rh_0 .	O	+	O	+	+	2 1
Rh_1Rh_2	+	+	+	+	+	11·5
rh .	O	O	O	+	+	15·1
rh′rh . .	+	O	O	+	+	0 76
rh″ .	O	O	+	+	+	0 9

Beyond this stage the subject becomes extremely complicated and even controversial, and should be studied with the aid of more specialized textbooks.

The author would like to thank Mrs Prentice for her help with the illustrations in this Chapter.

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The difference in water content between males and females is due to the greater fatness of the female, and it has recently been recognized that the fat content of the body may markedly affect the proportion of water by weight in the body although not the total quantity of water. When the fat content of a body increases the density of that body diminishes and buoyancy increases; in other words the specific gravity decreases. Specific gravity can be measured by weighing a body in air and in water, and from specific gravity fat content can be calculated. Behnke (1942) found that an increase in fat content impaired the physical efficiency of divers at great depths and of aviators at extreme altitude; it is well known that obese patients are poor subjects for surgical operations and suffer a higher incidence of post-operative complications than lean patients. What is also important is that estimates of total water content based on body weight are inaccurate unless some allowance is made for the variations in fat content between individuals. Behnke measured the fat and water content of a large number of men and postulated a basic body structure of more or less constant composition which he termed the "lean tissue mass," consisting of 70 per cent water, 20 per cent solids and 10 per cent structural fat. On the lean tissue mass, which remains fairly steady in individuals of similar height, age, and sex, a variable quantity of fat may be superimposed. A similar basic type of composition has been found also in other species of animal. When fat is superimposed on the basic "lean tissue mass" total body weight rises although there is comparatively little change in the total content of water, sodium, potassium, or other components of the lean tissue mass. One important effect of increasing the fat content of the body is thus to reduce the percentage of water and of other constituents in the body; when estimates of water or ionic content are made by calculation based on normal content per kilogram body weight, the results are too large in fat individuals and the excess may be up to 30 or 40 per cent. This sort of error may lead to the administration of unnecessarily large volumes of fluid and of electrolytes. Since direct calculations of total body water content from the observed body weight of a particular person may be very misleading unless suitable allowance is made for the fat content of that person, McCance and Widdowson (1951) have suggested that such calculations should be based not on the actual measured weight of the patient but rather on their ideal weight. This is a function of sex, height, and age and can be obtained from standard tables.

Total Content of Sodium and Potassium

The distribution of water in the body is largely determined by the distribution of the ions, such as sodium and potassium, with which it is associated in the body fluids. This close association also implies that the total quantity of water in the body is related to the total quantity of these ions. Although sodium and potassium are undoubtedly the most active cations in the body they represent only a small proportion of the total cations in the body. Total quantities of sodium and potassium in the body have been estimated by the dilution technique using their radioactive isotopes as tracer substances. This method involves the injection into the body of small quantities of radioactive sodium and potassium, and the subsequent measurement of the degree to which these radioactive materials have been diluted in the total mass of sodium and potassium in the body. From this the exchangeable sodium or potassium can be calculated; this is the total quantity of sodium and potassium which is present in the body in such a state that its ions can exchange with the radioactive ions which have been injected. A large number of measurements of

CHAPTER XIII

FLUIDS AND ELECTROLYTES

A. W. WILKINSON

ADVANCES in surgical and anæsthetic techniques have so increased the scope and magnitude of surgical operations that the margin between survival and death has been much reduced. It follows that many patients pass some precarious post-operative days during which the balance may readily be disturbed in several ways. In these circumstances and in such patients, post-operative treatment must be planned against a background of knowledge of the normal effects of injury and the influence of infective and other complications The importance of the prevention or limitation of abnormal losses of body fluid should be recognized, and sound therapeutic decisions depend on some knowledge of the composition of the normal body and the ways in which this is distorted by disease.

Recent advances in our knowledge of cellular as well as of whole body composition and function have led to radical revisions in earlier conceptions of the behaviour in the body of such clinically important constituents as water, sodium, and potassium. The clinical application of these new physiological concepts is long overdue.

TOTAL CONTENT AND DISTRIBUTION OF WATER, SODIUM, AND POTASSIUM

The composition of the human body has been widely studied in a large variety of subjects of both sexes at various ages. The total content of water, sodium, potassium, and some other constituents has been measured both by variations of the dilution principle employing either stable or radioactive isotopes and other tracer substances, and by studies on the composition of cadavers. Whereas differences between the results of studies of the same constituent by different methods emphasize the need for cautious interpretation, it is nevertheless now possible to make an estimate of the normal composition of a particular individual with sufficient accuracy for clinical purposes, and thereby to avoid both excessive and inadequate treatment

Content and Distribution of Water

The total body water has been measured in normal subjects by the dilution technique using various tracer substances, including deuterium, tritium, antipyrine, and urea Variations in the results with different tracers may be due to their differing rates and degrees of diffusion through the total mass of water in the body. With tritium and deuterium similar results have been obtained of 60 to 62 per cent of body weight in adult men and of 50 per cent in women, compared with 56 per cent and 48 per cent respectively with antipyrine. Edelman *et al.* (1952) judged that the average total water content of healthy adults was 61 per cent of total body weight in males and 54 per cent in females. They found also that the unusually high water content of the newborn child (77 per cent of body weight) fell during the following 10 years to about 59 per cent.

recent estimates of intracellular sodium concentration have been higher than this, but when allowance is made for the quantity of sodium present in bone, a figure of 15 mEq. per litre for soft tissues excluding bone is obtained which agrees well with the estimate of Hastings. On the basis of present knowledge it is possible to distribute the total sodium and potassium in the body as is shown in Table 1. The very large quantity of sodium in the bones is striking, there being as much here as in the rest of the body, but only half of the sodium of the skeleton is in a state which allows it to take part readily in the exchanges of sodium with other parts of the body.

TABLE 1. PARTITION OF BODY FLUIDS, SODIUM, AND POTASSIUM[1]
70 Kg. man (11 st. or 154 lb.)
Total body water = 60 per cent. Body weight = 42 litres

	Extracellular Fluid		Intracellular Fluid	
	Plasma	Interstitial Fluid	Soft Tissues	Bone
Total body water (%)	7	21	60	10
Volume (litres)	3	9	26	4
Sodium	43·4% of total 38·6 g. or 1,680 mEq. Av. 140 mEq./litre		9% of total 8 g. or 390 mEq. Av. 15 mEq./litre	47·4% of total 42·3 g. or 1,840 mEq Av. 460 mEq./litre
Potassium	2% of total 2·34 g. or 60 mEq Av. 5 mEq./litre		98% of total 130 g. or 3,360 mEq Av. 112 mEq./litre	

Subdivisions of Body Water

The water in the body can be conveniently divided into the arbitrary intracellular and extracellular fluids. *The extracellular fluid is subdivided into interstitial fluid and plasma.* These subdivisions are clinically useful, but it is important to recognize that they are arbitrary divisions and that in the living body water is not confined within compartments in any permanent way, but at all times is moving rapidly between cells and their environment and between different parts of that environment.

Intracellular Water. This is the largest subdivision of the total body water, amounting to 70 per cent. Intracellular water forms part of the protoplasm of the cells and is associated with the main intracellular cation potassium and with phosphate the main intracellular anion. The intracellular water has a complex distribution in many small cellular compartments separated from each other by two cell membranes and often in addition by a layer of interstitial fluid. All exchanges of intracellular fluid take place

exchangeable sodium and potassium have been made. Moore *et al.* (1954) combined their own data with those of Forbes and Perley (1951) and concluded that in healthy male adults total exchangeable sodium amounted to 42·1 mEq. per Kg. body weight and total exchangeable potassium to 46·3 mEq. per Kg. body weight. The expression of concentrations of constituents of fluids as milligrams per 100 ml. does not allow of comparison of the biological activity of these constituents since in this way only the weights of substances are compared. The use of the term milliequivalent is gradually becoming more common and has the advantage of comparing directly the biological activity or value of individual constituents. To many clinicians the introduction of the milliequivalent has seemed merely another unnecessary barrier to their understanding of the already too complicated new world of fluid physiology; this convention however permits the direct comparison of the concentrations of individual ions and is essential to the proper understanding and management of disturbances in the composition of body fluids. Its adoption requires some change of heart as well as of outlook and can be eased by the simultaneous expression of concentrations both as milligrams per 100 ml. and milliequivalents per litre. Biological activity depends mainly on the "chemical equivalence" of an element. The equivalent weight of an element is that quantity of it (expressed in grams) which will react with or displace from combination one gram of hydrogen; equivalent weight is also equal to the atomic weight divided by the valency. A milliequivalent is the equivalent weight of an element expressed in milligrams. Milligrams are converted to milliequivalents by dividing by the equivalent weight. To convert milligrams per 100 ml. to milliequivalents per litre the first step is to multiply by 10 to convert to milligrams per litre; this figure is then divided by the equivalent weight.

$$\text{Mg. per 100 ml.} \times 10 = \text{mg. per litre.} \quad \frac{\text{Mg. per litre.}}{\text{equivalent weight.}} = \text{mEq. per litre.}$$

for sodium 330 mg per 100 ml. = 3300 mg. per litre. $\frac{\text{3300 mg. per litre.}}{23} = 143$ mEq. per litre.

In a typical 70 Kg. male adult, the exchangeable sodium amounts to 2,947 mEq. of sodium and exchangeable potassium to 3,241 mEq. of potassium. Since 95 per cent of the total body potassium can exchange with isotopic potassium, the total content of potassium is in the region of 3,400 mEq. (133 g.). In the case of sodium however, one-quarter of the body content situated in the bones is not exchangeable; from this estimate and from the figure for exchangeable sodium it can be calculated that the total body content of sodium is about 3,920 mEq. (90 g.).

Only about 2 per cent of the total potassium is in the extracellular fluid at a concentration of about 5·0 mEq per litre (19·5 mg. per 100 ml.); 98 per cent of the total potassium is in intracellular fluid, largely in skeletal muscle, at a concentration of about 110 mEq. per litre. Until recently, it has been assumed that there was little sodium in the intracellular fluid, the bulk of the total body content being extracellular. The results of dilution experiments have now made it necessary to ascribe a different distribution of sodium in the body. At a concentration of 140 mEq. per litre (322 mg. per 100 ml.) there are 1,680 ml. of sodium in the 12 litres of extracellular fluid. Hastings (1941) estimated that the intracellular sodium concentration was 16 9 mEq. per litre. More

recent estimates of intracellular sodium concentration have been higher than this, but when allowance is made for the quantity of sodium present in bone, a figure of 15 mEq. per litre for soft tissues excluding bone is obtained which agrees well with the estimate of Hastings. On the basis of present knowledge it is possible to distribute the total sodium and potassium in the body as is shown in Table I. The very large quantity of sodium in the bones is striking, there being as much here as in the rest of the body, but only half of the sodium of the skeleton is in a state which allows it to take part readily in the exchanges of sodium with other parts of the body.

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[1] This scheme of distribution is arbitrary and is based on standard assumed volumes for plasma, interstitial fluid, and intracellular fluid. The [illegible]
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water loss plays an important part in dissipating the heat produced by metabolism, and thus in the regulation of body temperature, it is essential for survival. It is the inevitable primary water requirement of the body, and continues undiminished in spite of abnormal losses of body fluids and the formation of urine.

Sweat is the secretion of sweat glands and is an accessory means of cooling the body surface and so of dissipating the heat of metabolism. Sweating may be obvious when the rate of formation exceeds the rate of evaporation but often sweat evaporates as fast as it is secreted and so is not noticed.

Newburgh *et al.* (1937) found that there was little variation in the rate of insensible water loss in lightly clad men over a wide range of temperature. When a man is comfortable in his environment about a quarter of the total heat produced in the body is lost by insensible water loss, even when up to 6 per cent of the body weight has been lost by dehydration or when the caloric consumption varies from 2,200 to 3,600 per day. Estimation of insensible water loss from energy expenditure is more directly related to the problem of heat production and dissipation, and possibly more closely approaches the real loss but gives a higher value than other methods. For example, a man metabolizing 2,500 calories per day and dissipating one-quarter of his heat production by insensible water loss would have to lose $\frac{2{,}500}{4} \times \frac{1}{0{\cdot}58}$ ml. of water per day = 1,077 ml. This method of estimation does not take any account of body weight or height. Dubois (1927) estimated the insensible water loss to be 0·5 g. water per Kg. body weight per hour in adults (840 g. water for a 70 Kg. adult). Gamble (1947) made a similar estimate after measuring the weight loss of normal adults under varying conditions. For clinical purposes the figure of 0·5 g. per Kg. per hour is usually used as it is more convenient to weigh the patient than to measure energy consumption, either by estimating total calorie intake or the oxygen consumption. In computing the water requirements of surgical patients allowance is seldom made for insensible water loss and it is fortunate that the human body is so well able to tolerate moderate degrees of water depletion. Another important practical aspect of insensible water loss is the state of bodily comfort which depends on the adequate dissipation of body heat which in part depends on this type of water loss. When the atmosphere of the operating theatre becomes oppressively hot it is an indication of an increase in temperature or humidity which will also affect the unconscious patient, whose insensible water loss is then less likely to be adequate and the consequent sweating will increase water loss by the patient.

The surface area of infants and young children is larger in relation to their body weight than is the case in older children and adults. This leads to a higher rate of insensible water loss per Kg. body weight, which has been estimated by Benedict and Root (1926) to be as high as 1·3 Kg. body weight per hour.

Sweat. The sweat glands are partly under the influence of the adrenal cortical hormones and the composition of sweat may vary widely. In a normal subject sweating moderately, sweat may contain 5 mEq. of potassium and 50 to 100 mEq. each of sodium and chloride per litre. The content of sodium and chloride falls when the body becomes deficient in these substances, changes in their concentrations following fairly closely similar changes in the urine. The volume of sweat secreted varies with the nature of the environment and the work done. Potassium concentration in the sweat changes little. When sweating is copious, water can be replaced by drinking, potassium is replaced by

through the extracellular fluid, and thus depend on the maintenance of an adequate volume of environmental extracellular fluid. In addition the composition of the extracellular fluid must be maintained within narrow limits if cell function is not to be disturbed. The volume of intracellular fluid can be measured only indirectly by finding the difference between total body water and extracellular fluid volumes. Attempts to follow closely from day to day changes in intracellular fluid volumes and composition are limited by the difficulties and errors associated with repeated measurement of total body water and extracellular fluid volumes.

Extracellular Water. This amounts to about 28 per cent of the total body water and is subdivided into the intravascular portion (7 per cent of total body water) and interstitial portion (21 per cent of total body water). For the purposes of arbitrary division, the intravascular fluid or plasma lies within the blood vessels in the same way as interstitial fluid lies outside the blood vessels amongst the cells of the tissues of which it is the immediate environment. In both these subdivisions however, sodium is the most important cation and the content of potassium is very small. Chloride and bicarbonate are the predominant anions. Apart from the very large protein content of intravascular fluid there are only small differences in chemical composition between this fluid and interstitial fluid. Plasma volume may be measured by the dilution of the blue dye T1824 which remains the most convenient method for clinical use. Other methods also depend on the dilution of a substance which remains in circulation within the vessels. Extracellular fluid volume can be measured by the dilution of substances which pass freely through the capillary walls but do not enter the cells of the tissues. Suitable substances are thiocyanate or inulin, but it should be remembered that none of these substances gives entirely accurate measurements of the extracellular fluid volume.

Water Balance

Water balance exists when the daily intake equals the output or loss of water by various routes. In health, intake normally closely follows variations in output, but in disease and especially during the abnormal losses of body fluids which may complicate surgical operations, water balance may be greatly disturbed. The normal daily requirements are best judged by what is known of the normal outputs and losses of water from the healthy body.

Water Loss

(*a*) Extrarenal.
- (i) Insensible water loss through skin and in the expired air.
- (ii) In fæces.
- (iii) As sweat.

(*b*) Renal.

Extrarenal Water Loss

Insensible Water Loss. The expired air is saturated with water vapour and the rate of loss of water in this way is related to the depth and rate of respiration. The loss of water by diffusion of water vapour through the skin depends on the difference in water content between the body and the surrounding air; the rate of such loss varies with the temperature of the body and thus with metabolism, with the humidity and temperature of the environment, and with the clothing or bedding covering the body. Because insensible

water loss plays an important part in dissipating the heat produced by metabolism, and thus in the regulation of body temperature, it is essential for survival. It is the inevitable primary water requirement of the body, and continues undiminished in spite of abnormal losses of body fluids and the formation of urine.

Sweat is the secretion of sweat glands and is an accessory means of cooling the body surface and so of dissipating the heat of metabolism. Sweating may be obvious when the rate of formation exceeds the rate of evaporation but often sweat evaporates as fast as it is secreted and so is not noticed.

Newburgh *et al.* (1937) found that there was little variation in the rate of insensible water loss in lightly clad men over a wide range of temperature. When a man is comfortable in his environment about a quarter of the total heat produced in the body is lost by insensible water loss, even when up to 6 per cent of the body weight has been lost by dehydration or when the caloric consumption varies from 2,200 to 3,600 per day. Estimation of insensible water loss from energy expenditure is more directly related to the problem of heat production and dissipation, and possibly more closely approaches the real loss but gives a higher value than other methods. For example, a man metabolizing 2,500 calories per day and dissipating one-quarter of his heat production by insensible water loss would have to lose $\frac{2{,}500}{4} \times \frac{1}{0{\cdot}58}$ ml. of water per day = 1,077 ml. This method of estimation does not take any account of body weight or height. Dubois (1927) estimated the insensible water loss to be 0·5 g. water per Kg. body weight per hour in adults (840 g. water for a 70 Kg. adult). Gamble (1947) made a similar estimate after measuring the weight loss of normal adults under varying conditions. For clinical purposes the figure of 0·5 g. per Kg. per hour is usually used as it is more convenient to weigh the patient than to measure energy consumption, either by estimating total calorie intake or the oxygen consumption. In computing the water requirements of surgical patients allowance is seldom made for insensible water loss and it is fortunate that the human body is so well able to tolerate moderate degrees of water depletion. Another important practical aspect of insensible water loss is the state of bodily comfort which depends on the adequate dissipation of body heat which in part depends on this type of water loss. When the atmosphere of the operating theatre becomes oppressively hot it is an indication of an increase in temperature or humidity which will also affect the unconscious patient, whose insensible water loss is then less likely to be adequate and the consequent sweating will increase water loss by the patient.

The surface area of infants and young children is larger in relation to their body weight than is the case in older children and adults. This leads to a higher rate of insensible water loss per Kg. body weight, which has been estimated by Benedict and Root (1926) to be as high as 1·3 Kg. body weight per hour.

Sweat. The sweat glands are partly under the influence of the adrenal cortical hormones and the composition of sweat may vary widely. In a normal subject sweating moderately, sweat may contain 5 mEq. of potassium and 50 to 100 mEq. each of sodium and chloride per litre. The content of sodium and chloride falls when the body becomes deficient in these substances, changes in their concentrations following fairly closely similar changes in the urine. The volume of sweat secreted varies with the nature of the environment and the work done. Potassium concentration in the sweat changes little. When sweating is copious, water can be replaced by drinking, potassium is replaced by

through the extracellular fluid, and thus depend on the maintenance of an adequate volume of environmental extracellular fluid. In addition the composition of the extracellular fluid must be maintained within narrow limits if cell function is not to be disturbed. The volume of intracellular fluid can be measured only indirectly by finding the difference between total body water and extracellular fluid volumes. Attempts to follow closely from day to day changes in intracellular fluid volumes and composition are limited by the difficulties and errors associated with repeated measurement of total body water and extracellular fluid volumes.

Extracellular Water. This amounts to about 28 per cent of the total body water and is subdivided into the intravascular portion (7 per cent of total body water) and interstitial portion (21 per cent of total body water). For the purposes of arbitrary division, the intravascular fluid or plasma lies within the blood vessels in the same way as interstitial fluid lies outside the blood vessels amongst the cells of the tissues of which it is the immediate environment. In both these subdivisions however, sodium is the most important cation and the content of potassium is very small. Chloride and bicarbonate are the predominant anions. Apart from the very large protein content of intravascular fluid there are only small differences in chemical composition between this fluid and interstitial fluid. Plasma volume may be measured by the dilution of the blue dye T1824 which remains the most convenient method for clinical use. Other methods also depend on the dilution of a substance which remains in circulation within the vessels. Extracellular fluid volume can be measured by the dilution of substances which pass freely through the capillary walls but do not enter the cells of the tissues. Suitable substances are thiocyanate or inulin, but it should be remembered that none of these substances gives entirely accurate measurements of the extracellular fluid volume.

Water Balance

Water balance exists when the daily intake equals the output or loss of water by various routes. In health, intake normally closely follows variations in output, but in disease and especially during the abnormal losses of body fluids which may complicate surgical operations, water balance may be greatly disturbed. The normal daily requirements are best judged by what is known of the normal outputs and losses of water from the healthy body.

Water Loss

(*a*) Extrarenal.
- (i) Insensible water loss through skin and in the expired air.
- (ii) In fæces.
- (iii) As sweat.

(*b*) Renal.

Extrarenal Water Loss

Insensible Water Loss. The expired air is saturated with water vapour and the rate of loss of water in this way is related to the depth and rate of respiration. The loss of water by diffusion of water vapour through the skin depends on the difference in water content between the body and the surrounding air; the rate of such loss varies with the temperature of the body and thus with metabolism, with the humidity and temperature of the environment, and with the clothing or bedding covering the body. Because insensible

Thirst. Since Claude Bernard (1856) showed by experiments on animals with œsophageal or gastric fistulas that thirst was probably not a sensation localized and confined to the mouth and pharynx but a response to some general demand to increase the water content of the body, evidence has accummulated in support of this conception and against the theory of Cannon (1918) that thirst had its origin locally in a dry mouth. It has been repeatedly shown that the injection of hypertonic solution of sodium salts causes intense thirst. The increase in osmotic pressure which follows such injections is larger than that obtained with solutions of urea of similar concentration, and thirst is induced when blood osmotic pressure rises by 1 to 2 per cent, an amount similar to that which causes the release of antidiuretic hormone. When water alone has been lost, restoration of the body content of water depends simply on drinking enough water. Pure water depletion is rare and it is usual especially in clinical practice for water depletion to be accompanied by varying degrees of sodium and potassium loss. When water and sodium have been lost they must be restored in quantities which are at least in proportion to those lost if they do not exactly equal the losses; if sodium is not replaced in addition to water, the tonicity of extracellular fluid will be reduced until the excess water is excreted. It is remarkable that the loss of sodium and water in the proportions in which they exist in extracellular fluid does not cause thirst; if thirst did follow such a loss, the subsequent drinking of water would lead to dilution of the extracellular fluid. There is evidence that thirsting men and animals roughly measure the quantity of fluid they drink in the pharynx (Adolph, 1947); when allowed free access to water their water deficit is almost exactly replaced by drinking. The sensation of thirst can be relieved temporarily by wetting the throat with ice cold water and lastingly by putting enough water into the stomach through a tube.

The intense thirst which is experienced soon after severe injuries by shocked patients usually subsides when blood volume is restored by transfusion. This kind of thirst seems to be related to the acute reduction of blood or plasma volume and may be due to the shifts of intracellular fluid which is part of the compensatory response to bleeding or loss of plasma. After major surgical operations even when blood loss has not been severe, or has been completely replaced, severe thirst is usually experienced from 6 to 12 hours after operation and lasts for 48 hours or more and may continue for 6 or 7 days in patients who receive prolonged intravenous infusions. This post-operative thirst can be relieved only for a matter of minutes by the consumption of water, tea, or other fluids and is not affected beneficially by the intravenous infusion of glucose solution or isotonic saline (Wilkinson, 1956). Since the period of greatest intensity of thirst corresponds with the time when potassium is being lost in large quantities from the cells, it is possible that it is due to an intense intracellular dehydration and is a normal sequel to injury.

SODIUM

Normal Content and Distribution

The 90 g. (3,913 mEq.) of sodium in the typical adult male weighing 70 Kg. is distributed as shown in Table 3. Less than half of the total (44 per cent) is in the extracellular fluid and only 9 per cent is in the soft tissues, but all of this sodium readily takes part in the normal continuous interchange of sodium between the various parts of the body. The bones contain 47 per cent (42·3 g.) of the total body sodium and of this only

that consumed in the food, but the much larger losses of sodium and chloride must be replaced by the consumption of extra sodium chloride.

Fæcal Water Loss. This depends on the dryness of the fæces when passed and so on the rate of passage of material through the intestine. On a normal diet the average loss of water in the fæces is about 200 ml. per day, but during fasting the stools are small and contain little water. When many loose stools are passed in ulcerative colitis or when much mucus is lost in malignant disease of the colon or rectum, a litre or more of water and large quantities of sodium, potassium, and chloride may be lost each day.

Renal Water Loss. About 180 litres of fluid are filtered from the blood passing through the kidneys each day. About 85 per cent of this filtrate is absorbed isosmotically in the proximal convoluted tubules and most of the remainder is absorbed in the distal tubules leaving rather less than 1 per cent to form the urine. The minimum volume of water required by the kidneys each day to excrete completely the products of metabolism and of excessive intake in food and drink depends on the total quantity and nature of the solutes to be excreted, the "osmotic" or "solute load," and the ability of the kidneys to produce a concentrated urine. The solute load depends on the type and quantity of food consumed and the metabolic state; it is increased by tissue catabolism after injury and in many diseases, and by ketosis when fat metabolism is incomplete.

TABLE 2 TOTAL MINIMUM DAILY REQUIREMENTS OF WATER (70 KG ADULT)

Insensible water	70 Kg × 0 5 g per hour × 24 = 840 ml
Fæcal	= 200 ml.
Urine	= 500 ml.
Total	= 1,540 ml.

Water Intake. In a temperate climate the daily consumption of water by drinking may be as little as a pint (560 ml) but the average consumption by patients in hospital is *about 800 to 1,000 ml. The wide individual variation in water intake and turnover* receives too little recognition or respect. It may be as great a hardship and more harmful and even dangerous for elderly patients to be forced to drink 5 or 6 pints a day as for others to do without water entirely On an ordinary mixed diet about 12 g. water are produced for each 100 calories, equivalent to over 200 g water per day, and the water content of solid food varies from 60 to 95 per cent of its weight.

Regulation of Water Content of the Body

Of the organs concerned with water exchange the kidneys alone play an active part in regulation of the water content of the body. Insensible loss of water is a passive process which depends on the different water contents of the body and its environment and on the rate of heat production. Water output by the kidneys is controlled by the antidiuretic *hormone of the posterior lobe of the pituitary gland; the production of this hormone* depends on impulses set up in osmoreceptors which are sensitive to changes in the water content of the blood Restriction of water intake or excessive loss of body water leads to antidiuresis and oliguria Dilution of the blood by the ingestion or administration of a large volume of water leads to inhibition of hormone production, and after a delay during which existing hormone is destroyed there is an increase in urine volume; this diuresis can be stopped by the injection of antidiuretic hormone.

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45 per cent (19·0 g.) is exchangeable with isotopic sodium, that is to say only 45 per cent is readily available to take part in active movements of sodium in the body. The remaining 55 per cent of the bone sodium is combined in the crystal lattice of bone in such a way that it is not easily mobilized and does not appear to take part in acute shifts of body sodium. *Nevertheless there is enough readily available sodium in bone to act as a* convenient source during acute losses of sodium, and it seems likely that mobilization from

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Extracellular fluid	44	39·6	1,721	all	74% total 66 g. 2,900 mEq
Intracellular fluid . .	9	8·1	352	all	
Bone .	47	42·3	1,839	45% = 19·0 g. 827 mEq	

bone is one of the ways in which the concentration of sodium in the extracellular fluid is preserved. There are no stores of sodium in the body in the sense that fat can be considered to be stored; the available sodium in bone is a normal constituent the removal of which during acute disturbances of the volume or composition of the extracellular fluid probably causes some structural alteration in the bone. The maintenance of an adequate volume of extracellular fluid as an environment for the cells is clearly a condition of survival of the multicellular organism; it is equally important however, that the concentration of the solutes in extracellular fluid also should be maintained within narrow limits if cell function is to remain normal. Sodium is the most important cation in the extracellular fluid.

Renal Regulation of Sodium. The kidneys are the chief means by which the sodium content of the body is maintained; when sodium intake exceeds the extrarenal losses the excess is excreted in the urine, and when sodium intake is inadequate or ceases, the loss of sodium in the urine is more or less completely prevented by absorption of the sodium in the renal tubules. At an average glomerular filtration rate of 120 ml. per minute only 0·5 to 0·2 ml. of urine is formed per minute. At a plasma sodium concentration of 140 mEq. per litre, 16·8 mEq. sodium might be filtered each minute or up to 24,000 mEq. in 24 hours equal to fifteen times the total quantity of extracellular sodium, but only 100 mEq. sodium might be excreted in the urine. Most of these large quantities of filtrate and the contained sodium are absorbed in the proximal tubules with little change in the content of sodium, potassium, chloride or bicarbonate, but urea and some other substances are not reabsorbed and thus their concentration in the urine increases. The further modification of the partly concentrated glomerular filtrate during its passage through the distal tubules depends on selective absorption and on secretion by the tubular cells. The control of these distal tubular functions is only partly understood but is closely linked with the maintenance of chemical equilibrium in the body. In the distal tubules most of the remaining sodium is removed from the filtrate; the completeness of this extraction of sodium depends on many factors such as the total body content, the sodium intake, and

the infliction of injury or the presence of any form of active inflammation. There is also a normal variation in urinary sodium excretion between day and night. The ability to extract sodium from the glomerular filtrate is a characteristic of mature and of efficient renal function, and may be much diminished in some forms of renal disease. Newborn children in common with many other newborn animals are not as well able to conserve sodium in this way as are older children and adults (McCance, 1948). Infants are thus less well equipped to react to a deficient sodium intake by conservation and are peculiarly vulnerable to losses of body fluids.

Glomerular filtration rate varies with renal blood flow and both may fall when blood or plasma volume is reduced. In normal subjects the consumption or administration of water temporarily increases extracellular fluid, and plasma volume and hence glomerular filtration rate and urine formation, but sodium excretion is not always increased during such a water diuresis.

The control of sodium excretion and conservation is not well understood and will be further discussed later. Adrenal cortical extracts may cause sodium retention when the plasma sodium concentration is low, but they increase sodium excretion when the plasma concentration is raised. Administration of D.O.C.A. causes sodium retention regardless of the plasma sodium concentration and A.C.T.H. causes retention of sodium which after a few days may pass off. Whereas cortisone and hydrocortisone cause sodium retention, more recent synthetic agents of only slightly different structure have little or no effect on sodium excretion; it is evident that only small changes in the molecular structure of steroid hormones may cause large differences in renal function.

Normal Intake and Output of Sodium. The quantity of sodium consumed by normal adults varies widely with personal tastes and with racial and geographical dietary habits and preferences. In a temperate climate the daily intake may range from as little as 50 mEq. (3 g. sodium chloride) to 160 mEq. (10 g. sodium chloride), but the average is probably about 80–100 mEq. per day (5–6 g. as sodium chloride). Of this, 70–90 mEq. (4·5–5·5 g. as sodium chloride) may be lost in the urine and less than 10 mEq. in the fæces; the loss in sweat varies widely with the individual environment. It is fairly certain that under temperate conditions an intake of more than 160 mEq. sodium (10 g. as sodium chloride) per day is excessive and will lead to an increase in urinary sodium excretion. When 10 g. or more of sodium chloride are administered as isotonic saline during the first week after operation, the normal post-operative renal conservation of sodium leads to the retention of the bulk of the administered sodium and water and to an increase in body weight and may cause evident œdema.

Disturbances of Sodium Equilibrium

Changes in the distribution of sodium in the body occur after injury, in the presence of all other kinds of inflammation and in many diseases. In such circumstances the total quantity of sodium in the body may be altered, or changes in the water content of the body may alter the concentration of sodium in the body fluids. Disturbances of sodium equilibrium may be broadly classified as being due either to depletion or to excess of sodium; each of these types of disturbance may be subdivided into those which are real and are accompanied by a reduction or an increase in the total content of sodium, and those which are apparent in which the concentration of sodium in extracellular fluid but not the total body content of sodium is altered by variations in water content. Pure forms

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When a normal adult is deprived of water and food for 3 days (Nadal *et al.*, 1941) the body weight falls steadily, the mouth and throat become very dry and thirst is intense. The daily output of urine falls to about 600 ml. and its specific gravity rises to about 1,036. The urinary excretion of sodium is reduced but that of potassium unchanged. The plasma concentration of sodium and the packed cell volume of the blood do not change. When the water intake is resumed, recovery is rapid, the output of urine rises and its specific gravity falls; the body weight increases. Nadal and his colleagues also produced sodium depletion in normal adults by continuous duodenal aspiration with a Miller-Abbott tube; the intake of food was stopped but the free consumption of water was encouraged and glucose solution was administered by intravenous infusion. The body weight fell and 8 g. (348 mEq.) sodium were removed in the aspirated juices. The serum concentrations of sodium and chloride fell but the packed cell volume and plasma protein concentration rose; the urine volume remained high at an average of 1,430 ml. per day. The subjects became weak and apathetic, fainted when they sat up and their systolic blood pressures were reduced to 85 mm. Hg. They lost their appetites and were not thirsty and refused water when it was offered to them. No improvement occurred when suction was stopped but recovery followed rapidly when Ringer's solution was administered by intravenous infusion.

In the first experiment although the intakes of water and food were stopped, there was little change in the sodium content of the body because renal conservation reduced the urinary loss of sodium to a very small quantity. The continued insensible and renal losses of water were made possible by the replenishment of the extracellular fluid from the water of the cells; the resulting hypertonicity of the cells was probably responsible for the ensuing intense thirst and was partly overcome by the transfer of potassium from intracellular to extracellular fluid followed by its excretion in the urine. This experiment thus led to the depletion of body water content accompanied by the loss of intracellular potassium, but the volume and sodium content of the extracellular fluid were maintained. In the second experiment the removal of gastric and duodenal secretion resulted in the loss of a large quantity of sodium, chloride, and water and a small quantity of potassium (*see* Table 4). The water loss was replaced by drinking and infusion, thirst was not experienced, and the urinary volume was maintained. It is clear that the loss of a body fluid containing sodium cannot be compensated for simply by maintaining or even increasing the intake of water and that it leads to reduction in the extracellular fluid volume. Reduction in plasma volume, associated with an increased packed cell volume and in this form with an increased plasma protein concentration, is proportional to the reduction in extracellular fluid. Plasma volume cannot be preferentially maintained at the expense of interstitial fluid in sodium depletion because the capillaries are freely permeable to sodium and to water.

Sodium Depletion

(*a*) **Real.** Renal conservation is so effective that restriction of sodium intake alone is seldom an important factor in causing sodium depletion; in addition there must usually be some form of large abnormal loss of sodium from the body. The most important acute form of sodium depletion is caused by the rapid loss of large volumes of gastrointestinal secretions; the average composition of the individual secretions is shown in Table 4 but it is the loss of sodium and water and the consequent reduction in extracellular fluid volume which is the most serious disturbance. The severe form of this type

of any of these disturbances are probably very rare and in most clinical circumstances both sodium and water are lost.

(1) Sodium Depletion

(*a*) *Real* ("salt depletion"). This is due to the loss of sodium and usually also of water from the body; the extracellular (plasma) sodium concentration may fall, but when the sodium and water are lost in the same proportions as they occur in extracellular fluid (for example, in loss of plasma after burns) the extracellular sodium concentration may not change.

(*b*) *Apparent*. In the absence of sodium loss the extracellular sodium concentration is reduced by the administration of water more rapidly than it can be excreted by the kidneys. This is most common in elderly subjects after operation (water intoxication). Extracellular sodium concentration may be reduced also when a loss of sodium and water is replaced with water alone or with water and too little sodium (for example, when sweat loss is replaced by plain water).

(2) Sodium Excess

(*a*) *Real*. The sodium content of the body may be increased by the excessive ingestion or administration of sodium salts or by delayed, impaired, or altered renal excretion of sodium. If sufficient water also is ingested or administered, generalized œdema may develop.

(*b*) *Apparent*. When the total body water content is reduced (true dehydration), the extracellular sodium concentration may rise without there being any change in the total sodium content. Such a change in extracellular sodium concentration may also result from the loss of body sodium and water when the water loss is large in proportion to that of sodium.

Dehydration

This term is widely and loosely used to indicate the loss of water and mineral constituents from the body without any indication being given of the exact nature or source of the lost fluids. The unqualified use of words such as dehydration and shock leads only to confusion. That there are two kinds of so-called dehydration was clearly shown by Kerpel-Fronius (1935, 1938). In the one the loss of water unaccompanied by an equivalent quantity of sodium or potassium leads to thirst and oliguria; the water is derived mainly from the intracellular fluid, but some also is lost from the extracellular fluid. This form which may be called "pure water depletion" when it is due simply to the withholding of water is also known as "primary" or "simple" dehydration. In the other type there is a large loss of sodium as well as of water, derived mainly from the extracellular fluid, which leads to circulatory disturbances but not to thirst. This form is often known as "salt depletion," a term emphasizing less the predominant loss of sodium and water than the common mode of replacing such losses with isotonic saline; it is also known as "secondary" or "extracellular" dehydration since it affects mainly the extracellular fluid. Pure forms of either of these types of body fluid depletion are uncommon but various combinations of them are daily occurrences in modern surgical practice; for this reason detailed descriptions of the pure forms will be given and then the common clinical types of disturbance will be described.

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of sodium depletion is seen in Asiatic cholera, but very large losses of fluid may also occur in high small intestinal obstruction, acute dilatation of the stomach, high fistulas of the small intestine, ulcerative colitis, by diarrhœa from an ileostomy or a colostomy, or in the severe forms of diarrhœa which may follow the administration of the tetracycline series of drugs to starving patients. Large losses may also occur when drinking is permitted while repeated or continuous gastric aspiration is being carried out.

TABLE 4 COMPOSITION OF INTESTINAL SECRETIONS

Secretion	Concentration in mEq per litre				Volume per Day (ml)
	Na^+	K^+	Cl^-	HCO_3^-	
Gastric .	50	10	150	—	2,500
Intestinal .	140	10	100	25	3,000
Biliary .	140	5	100	30	500
Pancreatic	140	5	70	70	700
Cf plasma	140	5	103	25	—

A low sodium diet may become an important contributory factor in chronic sodium depletion in prolonged fever, in patients who have extensive granulating wounds, or when it is combined with the use of mercurial diuretics in the treatment of liver disease or in ulcerative colitis with œdema. Such a diet should not be combined with the administration of sulphonamide drugs which interfere with renal tubular absorption of sodium.

CLINICAL FEATURES. A detailed history of the nature and volume of the fluid loss is of the first importance but does not always give an accurate indication of the magnitude of the loss. The appearance of the patient may be characteristic: eyes deeply sunken in dark-ringed sockets, the face drawn and anxious; the skin is wrinkled and dry, the subcutaneous fat is lax and shrunken; the veins are small, constricted and poorly filled with slowly running thick dark blood. The state of the tongue depends on the relative proportions of water and sodium depletion which have occurred, and may vary from hard, brown, and dry when water loss is excessive, to a normal clean moist appearance when sodium depletion predominates. Similarly the volume and specific gravity of the urine depend very largely on the relative degrees of sodium and water depletion. The blood pressure may be long maintained within normal limits by vasoconstriction, but eventually falls to low levels and the pulse rate rises. Apart from hæmoconcentration there is seldom much change in the composition of the blood unless a large sodium loss is replaced by a solution containing an inadequate quantity of sodium The diagnosis nearly always depends on an accurate history and close bedside observation and examination of the patient. Only seldom is it necessary or desirable to delay the start of treatment until the results of chemical analyses of blood or urine are obtained, but specimens for analysis should always be secured at the outset as a base from which to try to judge the subsequent effects of treatment.

TREATMENT. When severe sodium depletion has led to reduction in extracellular fluid and plasma volume, the first measure to ensure survival is the rapid restoration of the circulating blood volume. This may require the rapid infusion of dextran followed by

isotonic saline. The loss of fluid also must be reduced or stopped as soon as possible, if necessary by operation. The detailed management of various types of acute and chronic loss of gastrointestinal fluid which may be encountered in surgical patients is dealt with later. In general, it may be said that the replacement of such losses is an individual problem in each patient, and treatment is best guided by the close observation of its effects on the patient, in particular on systolic and diastolic blood pressure, the state of peripheral venous filling, and the packed cell volume or hæmoglobin concentration of the blood. Various means of calculating the requirements of the individual patient have been proposed and may have some value as a preliminary indication of the probable amounts which may be needed, but close observation of response to treatment is undoubtedly the best method. Calculation of sodium requirements from the change in serum sodium concentration and the ideal plasma or extracellular fluid volume has been suggested; it is difficult to judge how much allowance should be made for mobilization of sodium from bone and for the effects of concentration and contraction in plasma volume, and such calculations are usually misleading and seldom helpful.

The dangers of unbalanced and ill-judged treatment of sodium and water loss are considerable, and even simple primary disturbances may be readily complicated and confused by equally simple remedies. In both excessive sweating and vomiting, the lost fluid contains sodium in a lower concentration than it exists in extracellular fluid so that water loss exceeds sodium loss. When repeated large losses by sweating or vomiting are replaced by water alone or by inadequate quantities of sodium, the cumulative sodium loss eventually leads to a sodium depletion which is aggravated by the continued administration of water. It is of interest that both water depletion and sodium depletion or dilution tend to have self-limiting secondary effects. When the intense thirst which follows simple water depletion can be satisfied by drinking, the water lack is relieved. Similarly when sodium and water depletion is treated by replacement of water alone the resulting sodium dilution leads to loss of appetite for water as well as food, and provided rectal or intravenous administration is not continued, the resulting abstinence from water and the continuing insensible water loss and urine formation gradually restore sodium concentration to within normal limits.

(*b*) Apparent. The production of sodium dilution by the replacement of a loss of sodium and water with water or with water and too little sodium has been described. The extracellular concentration of sodium may be reduced in the absence of any loss of sodium from the body by the rapid administration of a large volume of water. In normal healthy people the ingestion or infusion of a large quantity of water is followed by an early and complete excretion of the added water by the kidneys. It has been known for a good many years that especially after major operations and in elderly patients, the rapid administration of a large quantity of water is poorly tolerated. This appears to be due to the reduced capacity of the kidneys to respond by a diuresis in such circumstances, and a state of water intoxication may result.

Water Intoxication

Clinical Features. Large rectal infusions of tap water, rapid intravenous administration of glucose solution, and excessive post-operative drinking have each caused this disturbance. The rate of absorption or infusion appears to be the most important factor in causing dilution of the extracellular fluid, even rather small volumes causing severe

effects when infused very rapidly during the first three post-operative days; Zimmermann and Wangensteen (1952) observed symptoms and signs after the administration of only 3 or 4 litres of glucose solution over 24 hours. There is usually a marked increase in body weight. The condition is commoner after the age of 50 years and when renal function is poor, but it may also occur during severe infections or after operation in the newly born.

In the early stages appetite is lost and the patient is weak and disinterested; nausea, vomiting, and diarrhœa may follow. There may be twitching of the limbs, mental confusion, irritability, epileptiform seizures and rarely coma. These disturbances vary in severity, and in duration from a few hours to several days. At first a large volume of dilute urine is passed but this may be followed by oliguria and even anuria. Neurological disturbances are inconstant. The plasma concentrations of sodium, chloride, and bicarbonate are reduced, potassium also is usually reduced but may rise if oliguria is severe or during anuria. There is marked depression of the hæmoglobin and plasma protein concentrations.

Spontaneous recovery, which depends on the dissipation of the excess water by insensible vaporization or excretion as urine and perhaps to some extent as vomit or in loose stools, is naturally a slow process, and the patient may be in a confused and irritable state for a week or more. Recovery may be accelerated by raising the extracellular sodium concentration by the slow intravenous infusion of 200–400 ml. of hypertonic (5·85 per cent) saline. The infusion should be stopped when symptoms are relieved or when the urinary output is seen to increase. The too rapid injection of hypertonic saline may cause cardiac arrest or circulatory overloading. It has been suggested that the dose of sodium to be administered can be accurately judged from the observed extracellular (plasma) sodium concentration and the ideal normal water content of the patient. In practice however, it is usually safer to watch closely the effects of the infusion of hypertonic saline and stop when symptoms are relieved.

Sodium Excess

In health, when the daily intake of sodium is increased, this is followed by an increased excretion of sodium in the urine. In some forms of renal disease, the kidneys are incapable of responding sufficiently well to excrete large additional loads of sodium, and when renal functional impairment is severe the body sodium content may increase even when the daily sodium intake is deliberately reduced by dietary restrictions. After accidental or surgical injury, and during severe inflammation of other kinds, the kidneys normally conserve sodium very closely and the daily urinary loss of sodium is reduced to small quantities for up to a week (Wilkinson, 1956). Since this type of renal sodium conservation persists to a varying degree even when large quantities of sodium are administered by rectal, subcutaneous, or intravenous infusion, an increase in total sodium content is common during the early post-operative period when isotonic saline is administered (Stewart and Rourke, 1942; Moyer *et al.*, 1947). Even in normal healthy individuals there is a delay in the urinary excretion of the added sodium and water following the rapid intravenous infusion of 0·9 per cent saline.

Œdema is due to the accumulation of interstitial fluid and usually follows an increase in sodium and water contents of the body; it is important to recognize that œdema may also follow the excessive intravenous administration of 6 per cent glucose solution and is then associated with sodium dilution. It is often difficult to find the cause of œdema in surgical

patients. Reduction of the plasma concentration or total quantity of the plasma proteins, especially albumin, is commonly blamed and may be due to previous malnutrition or to protein depletion by chronic infection, prolonged discharge from large granulating surfaces in abscess cavities or burns; it may also be due simply to the dilution of the plasma volume following expansion of the extracellular fluid by the excessive administration of isotonic saline. Œdema may also be secondary to the retention of sodium induced by cortisone, A.C.T.H. or other steroid hormones. Œdema is associated with severe undernutrition, and is not uncommon in patients with ulcerative colitis, œsophageal obstruction and carcinoma of the alimentary tract. Large quantities of sodium and water may accumulate in the body before expansion of the extracellular fluid becomes clinically evident as œdema, with pitting on pressure over the sacrum or in the scrotum or lower limbs.

Œdematous patients still have to provide water for insensible water loss and urine formation, and it is important to maintain an adequate daily intake of water for these purposes while restricting the intake of sodium.

POTASSIUM

Normal Content and Distribution

The typical 70 Kg. adult male contains 3,411 mEq. (133 g.) of potassium, nearly 98 per cent of which (3,350 mEq.) is in the cells, mainly the skeletal muscles, and only about 2 per cent (60 mEq.) is in the extracellular fluid.

Intake and Output

On an average mixed diet the daily intake of potassium is about 50–75 mEq. (2–3 g.), a similar quantity is excreted in the urine, and a negligible quantity in the sweat. In addition, between 50 and 130 mEq. (2–5 g.) are daily secreted into and reabsorbed from the alimentary tract.

The renal treatment of potassium differs as widely from that of sodium as do the distributions and probable functions of these two elements in the body as a whole. The body content of sodium is carefully safeguarded by renal conservation when sodium intake is restricted or ceases or when there are abnormal losses of sodium from the body; only by so maintaining the total content of sodium can the volume and tonicity of extracellular fluid be preserved, and a normal fluid environment be ensured for the cells. The surge of potassium from the intestine which accompanies the absorption of intestinal secretions and the products of digestion of food is overcome by the rapid uptake of potassium by cells and little of this added potassium appears to overflow into the urine. When there is a generalized shift of potassium out of the cells, for example during the first 48 hours after injury, the tendency for the extracellular potassium concentration to rise is usually prevented by the rapid excretion of this mobilized potassium at a high concentration in the urine. Even in simple starvation, continuing protein catabolism leading to the breakdown of only 180 g. of fresh muscle per day would release 6 g. of nitrogen. With each gram of nitrogen 2·5 to 3·0 mEq. potassium are released and if this potassium is not promptly excreted by the kidneys the extracellular potassium concentration will rise; it is for this reason that in anuria the extracellular potassium concentration and the normal total extracellular content of about 60 mEq. may be doubled *in 4 or 5*

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accumulate and may eventually amount to as much as 25 per cent of the initial total body content of potassium. The intravenous infusion of saline and of glucose solution also causes a disproportionate loss of potassium.

The causes of potassium deficiency, any or all of which may be concerned in one particular patient, are as follows:

(1) Cessation or restriction of the intake of potassium combined with continued loss of potassium in urine.

(2) Proportionate loss with nitrogen from catabolized protein tissue in starvation, where food, and especially energy intake, is inadequate, or after injury.

(3) Disproportionate loss due to intracellular fluid loss because of

(*a*) inadequate water intake.

(*b*) loss of gastrointestinal secretions by vomiting, diarrhœa, or fistula.

Clinical Features. Because the development of severe potassium deficiency depends on the accumulation of repeated small daily losses, in addition to the continuing loss in the urine, there is usually a long history of loss of secretions and this should always cause suspicion that an overt disturbance may underlie the apparently normal appearance of the patient. The clinical picture varies widely and is easily recognized only in its severe forms when the most striking feature is intense drowsiness of gradual onset. Such a patient slumps to one side in bed with the head on one shoulder and is roused with difficulty, he opens his eyes slowly and with obvious effort, seldom understands what is said to him and appearing too tired to keep his eyes open, droops his eyelids and his head again. Speech is slurred and slow and he may stop in the middle of a sentence; some patients are irritable and bad tempered and there may be much change in personality, but after recovery, nearly all patients have no memory of the days when the clinical disturbance was most severe, even although they have remained conscious throughout the illness. There may be muscular weakness or incoordination and the deep reflexes are occasionally absent; swallowing may be difficult and liquids may be inhaled; incontinence of urine is common. Ileus with abdominal distension is found with post-operative potassium depletion. The skin is warm and dry and there may be a reddish flush on the cheeks and the backs of the hands. The peripheral blood pressure may be low but the veins are usually well filled provided sodium and water replacement is adequate. Changes in the electrocardiographic tracing vary widely and may be absent even in severe deficiency; when present, they are not related to the severity of the potassium depletion or to the serum potassium concentration. Amongst the changes which have been described are reduction in the magnitude of all waves, increased QT interval, decreased height, inversion or rounding and prolongation of T wave, depression of ST or invasion of P wave. Most of these changes may also be caused by alkalosis and changes in blood pH, but when due to potassium deficiency are rapidly improved by the administration of potassium salts.

The plasma potassium concentration depends on so many factors that it is often an unreliable index of the body content of potassium. The concentration at a particular moment depends on the rate at which potassium is being mobilized from or deposited in cells, or excreted in the urine, and also on changes in the volume of the extracellular fluid. Although the total body content is normal, the serum potassium concentration may be reduced when the extracellular fluid volume is rapidly increased by intravenous infusions

days. Survival after injury therefore depends as much on the rapid excretion of potassium mobilized from the intracellular fluid as it does on the renal conservation of sodium and the maintenance of the composition and an adequate volume of extracellular fluid.

Whether potassium is excreted in the urine appears to depend on how much is available for excretion from the extracellular fluid. The extracellular fluid content of potassium is related to the consumption of food and varies according to whether the cells are taking up or shedding potassium; this in turn is related to such factors as the rate of water intake and loss from the body, starvation, injury, and disease. Potassium excretion in the urine is increased by aldosterone, A.C.T.H., cortisone, desoxycorticosterone, P.A.S. and mercurial diuretics, and by the intravenous administration of solutions containing sodium salts, glucose or ammonium chloride.

The maintenance of a normal body content of potassium depends on the maintenance of an adequate daily intake of potassium in food. When potassium intake is restricted the kidneys do not conserve potassium as they do sodium, and excretion in the urine continues; this continuing urinary loss leads to slow depletion of the body content of potassium. This apparent renal inability to conserve potassium is possibly based on the need to continue to excrete potassium transferred from intracellular fluid during restriction of water intake, when the continuing requirements of water for insensible loss compel the mobilization of water from the cells to maintain the volume of the extracellular fluid.

Potassium Deficiency

Types of Potassium Loss. In starvation without restriction of water intake protein tissue is catabolized and there is a loss of potassium and nitrogen in the urine in the same proportion (2·5–3·0 mEq. potassium per gram of nitrogen) as that in which they exist in skeletal muscle (proportionate loss of potassium). During the restriction of water intake, water moves from the intracellular to the extracellular fluid and this is followed by the transfer of potassium to the extracellular fluid whence it is excreted in the urine. In these circumstances, the urinary loss of potassium is thus greater than that of nitrogen from catabolized tissue (disproportionate loss of potassium) since in addition to the potassium released by the catabolism of protein tissue it includes potassium mobilized with intracellular water. A disproportionate loss of potassium also accompanies the loss of any body fluid containing potassium. For example, the concentration of potassium in gastric and intestinal secretion, although low, may be up to twice that in extracellular fluid. In acute losses of such secretions the loss of potassium relative to that of sodium, chloride and water is small and can be readily replaced from the intracellular fluid. Although 25 per cent of the total extracellular sodium may be acutely lost, this is accompanied by the loss of only about 4 per cent of the total body potassium; in the treatment of such acute losses the emphasis is rightly on the re-expansion of the extracellular fluid volume by the rapid replacement of the lost sodium and water by the infusion of isotonic saline. With the resumption of a normal diet, the small loss of potassium is soon made good. When, for example, in pyloric stenosis, vomiting is repeated over a prolonged period there are large losses of gastric secretions and the intake of food is limited; similarly in infantile gastro-enteritis vomiting and diarrhœa restrict food intake and cause large losses of gastrointestinal secretions. In such circumstances replacement of the lost sodium and water by infusion of saline maintains the body content of water and sodium and extracellular fluid volume, but the repeated unreplaced small losses of potassium

The main indications for *the intravenous administration of potassium salts* are coma, difficulty in swallowing, nausea or continued vomiting; often however, the intravenous administration of only a small quantity, as little as 1 g. of potassium chloride (13 mEq. potassium) may be enough to restore consciousness or markedly improve the co-operation of the patient. To reduce the risk of the extracellular potassium concentration rising to a possible toxic level (27 mg. per 100 ml., 7 mEq. per litre) it is wise to ensure that the urine output is at least 20 ml. per hour (500 ml. per day) before the intravenous administration of potassium salts is begun, if necessary by the prior infusion of 500 ml. of 5 per cent glucose solution. The best indication of an excessive rise in extracellular potassium concentration is slowing of the heart and pulse rates; the administration of potassium should be stopped at once and replaced by 5 per cent glucose solution. The intravenous administration of potassium salts in effective concentrations is dangerous and should not be instituted without good reason after careful consideration of the risks and the possible advantages to be gained. The total dose and the rate of administration should be stated in writing and the infusion should be closely supervised by a house surgeon. In general, the patient should be carefully examined after 2 g. potassium chloride have been given. Recent suggestions that the daily intravenous administration of small quantities of potassium during the first few days after operation does not do any harm and may do some good, seem to be incompatible with the acceptance of the large amount of evidence bearing on the normal metabolic response to injury; such suggestions are unwise and may be dangerous, although the potassium is fortunately usually excreted.

When potassium deficiency is due to repeated vomiting, it is accompanied by severe extracellular alkalosis, and potassium chloride should be used in treatment. Provided the urine output exceeds 500 ml. per day, up to 2 g. potassium chloride (26 mEq. potassium) may be given over 4 hours by intravenous infusion using 350 ml. of a solution containing 5 per cent glucose and 0 55 per cent potassium chloride (74 mEq. per litre). Alternatively 20 ml. of 10 per cent potassium chloride solution are added to 500 ml. of 5 per cent glucose solution to make a solution containing 0 4 per cent potassium chloride (53 mEq. per litre of which 500 ml. are given). It is usually advisable to administer 500 ml. of 5 per cent glucose solution after each 500 ml. of solution containing potassium chloride and also such quantities of 0 9 per cent saline as are required to restore and maintain the volume of extracellular fluid. During intravenous administration up to 6 g. potassium chloride (78 mEq. potassium) may be given in the first 24 hours. As soon as the patient can drink and retain fluids, and his urine output exceeds 500 ml. per day, he should be given up to 12 g. potassium chloride per day (156 mEq. potassium) in doses of 2 g. potassium chloride every 4 hours at least until the plasma potassium concentration has returned to normal, the oral administration is then continued at a lower dosage (8 g. per day) for several days until a full diet is being consumed.

When potassium deficiency is due to losses in loose stools or in fistulous discharges, it is usually associated with acidosis. The need to supply additional sodium with a metabolizable anion is met by the addition of sodium lactate to solutions for intravenous administration (Darrow's solution). As soon as the patient is able to swallow, potassium citrate should be taken by mouth in 2 g. doses every 4 hours. An alternative mixture contains 1 g. each of potassium bicarbonate, acetate, and citrate dissolved in 8 ml. of water flavoured with fruit juice; taken every 6 hours this provides 116 mEq. of potassium per day.

or by the rapid deposition of glycogen after the administration of glucose and insulin. The serum potassium concentration may be raised in spite of a large body deficit of potassium when the extracellular fluid volume is reduced, for example by loss of intestinal fluids, especially if renal function is impaired or the output of urine is reduced. Persistent depression of the serum concentration is usually a feature of severe and prolonged potassium deficiency, whereas elevation of the concentration is most often found in association with renal failure or anuria. The normal range of potassium concentration in plasma or extracellular fluid is from 3·8–5·1 mEq. per litre (15·0–20·0 mg. per 100 ml.) and values of less than 3·5 mEq. (13·6 mg. per 100 ml.) or more than 7 mEq. per litre (27 mg. per 100 ml.) are usually considered to be abnormal. There is commonly an extracellular alkalosis and intracellular acidosis when potassium depletion by vomiting is severe, but extracellular acidosis accompanies depletion by diarrhœa or intestinal fistula. Respiration may become phasic when there is also severe alkalosis, or raucous and harsh with so-called air hunger in advanced acidosis.

The Diagnosis of Potassium Deficiency depends chiefly on the arousal of suspicion of its existence whenever there has been prolonged loss of gastrointestinal secretions and restriction of food intake, or the repeated intravenous administration of fluids which do not contain potassium, especially if this is the only source of water and energy. Diagnosis is most surely based on the history and clinical appearance; a low plasma potassium concentration or a typical change in the electrocardiographic tracing is of value in confirming the diagnosis but is seldom the only sign of deficiency, and too much emphasis should not be laid on these investigations.

Treatment. It is uncertain what proportion of the total normal content of potassium must be lost before the deficiency produces enough disturbance of function to become clinically obvious. Losses of 200 mEq. in 2 or 3 days are common after many uncomplicated major operations such as partial gastrectomy, and it is probable that even losses of 500 mEq. do not cause any ill-effects in previously normal people. In chronic losses of gastrointestinal secretions combined with a low potassium intake, the total deficit may amount to 25 per cent of the normal content or about 850 mEq. (33 g.) in a lean 70 Kg. adult male with a normal content of 3,400 mEq. (130 g.). The only way in which the total potassium content can be measured is by the dilution technique using radioactive potassium (^{42}K); this method is not suitable for routine use. The total quantity of potassium required to correct potassium deficiency in a particular patient must therefore be judged by the response to treatment A retrospective estimate of the original deficit can be made by measuring the proportion of the administered potassium which is retained in the body; from the total quantity ingested is subtracted all the potassium lost in the urine and in abnormal fluid losses during the period of treatment.

Because of the danger of a rapid increase in the potassium concentration of the plasma and extracellular fluid which is inseparable from the intravenous administration of solutions of potassium salts, the oral route should be used whenever possible. This danger is greater when the extracellular fluid volume has been acutely reduced by the rapid and unreplaced loss of gastric or intestinal secretions and when the output of urine is low. If the loss of secretions has been so extensive as to cause peripheral circulatory failure, dextran should first be injected, otherwise 0·9 per cent saline is sufficient, but the volume should be limited to a minimum because of the tendency of sodium to be transferred into the potassium-deficient cells.

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Potassium Retention

In health, the potassium content of the body cannot be excessively or dangerously increased by the consumption of potassium salts because the kidneys so promptly excrete the excessive added potassium. Potassium retention usually implies therefore an accumulation of potassium in the extracellular fluid; this may follow the administration of potassium salts because the rate of cellular uptake is slow in proportion to the rate of administration, and is usually combined with some impairment of renal function and reduction in urinary output. On the other hand, the release of intracellular potassium as the result of restriction of the intake of water or food, after injury or during infection, when combined with severe impairment of renal function leads inevitably to an increased extracellular content of potassium without change in the total body content. The intravenous infusion of potassium salts in too large quantity or at too fast a rate especially when urinary output is low, also may cause elevation of the extracellular potassium concentration.

The clinical features of potassium retention are indefinite and difficult to separate from the associated disease. There may be mental confusion, apathy and weakness. The peripheral circulation is poor, the skin is cold, pale, and cyanosed, the heart rate is slowed, the beats irregular, and cardiac arrest a common ending. Electrocardiographic changes are more common with a raised than with a low extracellular potassium concentration and may appear at plasma potassium concentrations of 7 mEq. per litre (27 mg. per 100 ml.) and are always present at 8 mEq. per litre (30 mg. per 100 ml.). The T wave is peaked and the duration of the Q.R.S. complex and the P.R. interval is increased.

Treatment consists in preventing any further increase in extracellular potassium content or concentration and in eliminating the accumulated potassium. If it is due to the intravenous administration of potassium salts, this should be stopped and the flow of urine promoted by the rapid infusion of 5 per cent glucose solution. In anuria the accumulation of potassium should be minimized by the reduction of cellular catabolism due to starvation by the daily consumption of at least 100 g. glucose. In addition potassium may be extracted from the body by the use of a suitable ion exchange resin (*see* p. 552).

EFFECTS OF PARTIAL AND COMPLETE STARVATION

The consumption of food and water is usually restricted if not stopped for 12 hours before and for a varying period after surgical operations; such restrictions have important effects, and their duration should therefore be reduced as far as possible. Gamble (1947) showed that when a healthy male adult was deprived of both water and food, about 200–300 ml. water were obtained from the oxidation of body fat and protein, but the remaining 1,300 ml. out of a total daily water requirement of about 1,500 ml. were obtained from the intracellular and extracellular fluids. The use of these fluids to satisfy essential water requirements was accompanied by the excretion of sodium and potassium in the urine, and the quantities of these two elements in the urine indicated the varying contributions made by intracellular and extracellular fluids. Thus sodium loss was high during the first day, but fell rapidly during the next 2 or 3 days, and from the fourth or fifth day onwards, the intracellular fluid was supplying most of the water used; potassium excretion continued almost unchanged or was increased. This expedient of transfer of water and potassium from the intracellular fluid allows extracellular fluid volume to be

maintained and water loss to continue for a much longer period than otherwise would be possible if the water were derived solely from the smaller total volume of the extracellular fluid. Experiments in animals have shown that death occurs when 40 per cent of the total normal body water content has been lost, which is equivalent to about 17 litres in a 70 Kg. man, and at 1,300 ml. per day would be lost in about 13 days.

When ample water is allowed but food is withheld, the continuing oxidation of fat and protein provides 200-300 ml. water and the remainder can be supplied by water to drink. Renal conservation prevents any large loss of sodium, but up to 500 ml. of body water are lost per day. When in addition to water the fasting adult is allowed 100 g. of glucose per day, the ketosis which usually appears on the second day of the fast is prevented, and protein catabolism is halved. As a result the solute load to be excreted in the urine also is halved and the minimum volume of urine to clear the body completely of metabolic end-products also is halved. Urinary sodium excretion may also be reduced by about half but potassium excretion is increased by one-sixth. No greater benefit results from the consumption of more than 100 g. glucose which is the optimum quantity both for the prevention of ketosis and the reduction of endogenous protein catabolism to the minimum of 40 g. per day. There is therefore good justification for the daily consumption of 100 g. glucose and abundant water by the starving uninjured subject.

EFFECTS OF INJURY

Local Tissue Change After Injury. All injuries lead to alteration in capillary permeability and the formation of an inflammatory exudate in the injured tissues. This exudate, rich in protein, is derived primarily from the plasma; after burning, it is the sole cause of the swelling of the injured part but in lacerated injuries, the effusion of whole blood also contributes to the swelling. After crushing or burning limbs, or handling the intestines of dogs, Blalock (1931) found that the volume of the local loss of fluid might be equal to 4 or 5 per cent of body weight or half the initial blood volume. The rate of lymph flow out of a burned limb may be increased up to eight times the normal (Fine and Seligman, 1943) and albumin crosses the capillary wall in the burned area as rapidly as sodium and can exert little osmotic effect within the vessels (Cope and Moore, 1944). These rapid rates of exudation from the capillaries and lymph flow out of injured limbs indicate that the accumulation of fluid in the tissues and the consequent swelling of the limb are due to the rate of formation of the exudate exceeding the rate of its removal; although fluid accumulates in the tissues, it is flowing through the extravascular space in large quantities and the inflammatory exudate is constantly changing its composition. Only when from about 24 hours or more after injury the rate of formation of the exudate declines, does the size of the inflammatory swelling also diminish. Since the accumulated fluid is derived from the plasma and not all severely injured animals or human beings die of shock after severe injury, even in the absence of treatment there must be some means of compensating for the large loss of fluid into the inflamed tissues. Ricca *et al.* (1945) found that the amount of fluid which collected in the hind limbs of dogs crushed by a Blalock clamp was greater than the measured reduction in plasma volume, and that although the sodium and water content was increased in injured muscle it was reduced in most of the uninjured tissues of the body. Similar observations were made by Fox and Baer (1947) who also found that the potassium content of injured cells was markedly reduced. There is clearly

a large shift of water and sodium into and of potassium out of injured tissues. Fine and Seligman (1943, 1944) have shown however, that changes in capillary permeability are confined to the injured area, and that even in severe shock after injury there is no generalized increase in capillary permeability in undamaged tissues. Capillary permeability remains increased in the injured tissues for from 3 to 5 days after injury (Cameron *et al.*, 1945), but the rate of fluid loss is early reduced by the increasing tension in the swollen tissues.

General and Metabolic Effects. *Even in the absence of infection,* severe injury is followed by loss of weight and wasting of fat and muscle which evidently cannot always be due entirely or even largely to starvation, toxæmia or the loss of body fluids in purulent discharges. The pioneer studies of Cuthbertson (1930) on patients with fractures have been followed by many other investigations into the chemical and hormonic basis of the biological response to injury, and there is now wide but not unanimous agreement regarding the broad pattern of behaviour after severe accidental or surgical injury. An understanding of the normal reaction uninfluenced by the effects of orthodox therapy is essential to the management of surgical patients after some major operations, and it should not be forgotten that many patients recover in spite of the treatment they receive.

Changes in Urinary Composition. When, after an operation such as partial gastrectomy, the intake of food and water is stopped for 48 hours, and then is gradually resumed, the volume of urine remains small for 48 hours (25 ml. per hour, 600 ml. per day) and then slowly increases towards the pre-operative level; urinary specific gravity is raised for a week or more. Oliguria is a normal response to severe injury even when there has not been a large loss of blood or plasma, but there may be wide individual variations both in the daily volume and concentration of the urine.

After injury, the composition as well as the volume of the urine changes. The urinary excretion of nitrogen begins to rise above the pre-operative range of 12–15 g. per day during the first post-operative day and may remain high for 6 days or more reaching a peak between the second and fifth days after surgical operations, and between the fourth and eighth days after fractures. About the end of the first week the nitrogen excretion declines but this tendency is to some extent offset by the consumption of a light or normal diet containing protein. Within 10 days of severe injury, 120 g. or more of nitrogen may be lost in the urine by a previously well nourished adult; this quantity of nitrogen is equivalent to that contained in 3 Kg. (6·6 lb.) of fresh muscle. Complications such as wound infection or thrombophlebitis, or the development of extensive granulations are associated with prolongation of the excessive urinary loss of nitrogen and of renal sodium conservation.

During the first 48 hours after operation, there is a large increase in the urinary output of potassium from less than 50 mEq per day before operation to 75–125 mEq. per day; this is followed by a reduction to below the pre-operative excretion which lasts for 10 days or more. In 2 or 3 days up to 200 mEq. (8 g.) of potassium may be lost, equivalent to the potassium in nearly 2 litres of intracellular fluid. During the first few days, there are also increased urinary losses of phosphorus and sulphur. These changes in urinary composition have been interpreted as being due to the breakdown of cellular protein and the excretion of its components in the urine. The increased outputs of potassium and phosphorus occur before those of nitrogen and sulphur; this may be due either to the

more rapid mobilization of potassium and water than of nitrogen, or to slower catabolism of the nitrogenous part of the protoplasm.

Reduction in the urinary output of sodium from the pre-operative daily quantity of more than 100 mEq. begins soon after and rarely even before operation, and only small quantities (less than 25 mEq. per day) are passed from the third to fifth days; thereafter the output varies but increases often to more than the pre-operative quantities during the second post-operative week. The urinary excretion of chloride follows the same pattern as that of sodium. Some of these varied changes in urinary compositions are shown in Fig. 207 which indicates the extraordinary alteration in renal function which follows injury such as an operation for partial gastrectomy and the stoppage of water intake for 48 hours. There is a large increase in urinary potassium concentration at the time when the kidneys are closely conserving sodium and in advance of the peak of nitrogen excretion (Wilkinson, 1956). A similar pattern is also found when moderate quantities of 0·9 per cent saline and 6 per cent glucose solution are administered by intravenous infusion during the first 2 days after operation. Where very large volumes of water (4 litres per day, Le Quesne and Lewis, 1953) are administered, there is distortion of the normal renal response to injury, oliguria lasts only 24 or 48 hours, sodium conservation also is of shorter duration, but potassium loss may be increased. There is no evidence that any benefit is derived from such very large intakes of water or that the resulting diuresis is necessary or of any value. It has also been claimed that the abundant transfusion of whole blood will reduce the call on intact tissues for the components of the repair process; this claim is not justified, for such free use of blood transfusion increases *rather* than diminishes the loss of sodium and potassium, and distorts but does not *fundamentally* change the normal response (Flear and Clark, 1955).

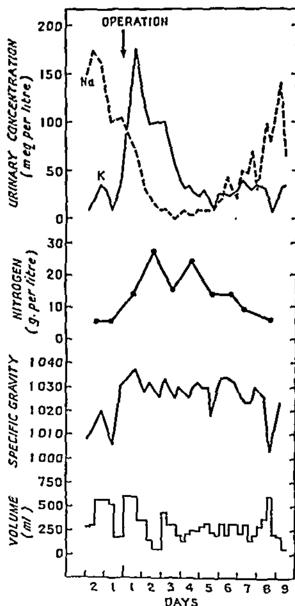


FIG. 207 Changes in urinary concentration of sodium, potassium, and nitrogen, specific gravity, and volume after partial gastrectomy with *restriction* of fluid intake Concentration of nitrogen refers to 24-hour pooled urine, but all other estimations were made on individual specimens of urine

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equally large increase in energy expenditure, which probably rises to well over 3,000 calories per day and requires the oxidation of 300–400 g. of fat.

For some years, evidence has been accumulating in support of the idea that the profound changes in total body composition and in the redistribution of body components which follow injury are largely dependent on or mediated by hormones secreted by the adrenal cortex. It is known that these hormones produce effects in uninjured subjects which are similar to those observed after injury. Recent advances in the isolation and chemical identification of cortical hormones and their derivatives, both in the blood and the urine of surgical patients, strongly support the belief that the tissues respond to the quantities of adrenal steroids circulating in the extracellular fluid surrounding the cells. While recognizing the effect of pain, fear, anæsthetic and other drugs, starvation, blood loss, local vascular changes, altered liver function, and antidiuresis, the recent investigations of Moore and his colleagues (Moore *et al.*, 1955; Steenburg *et al.*, 1956) indicate that the 17-hydroxycorticoids are of primary importance in the production of the changes in nitrogen metabolism. Variations in the duration of the high blood concentration of 17-hydroxycorticoids associated with different types of injury such as entirely soft tissue injuries by gastrectomy, fractures and burns have yet to be explained. It now appears that the body is well equipped to provide water for insensible water loss at even this enhanced rate as well as for urine formation; the increased potassium and reduced sodium excretion in the urine appear to be related to the larger output of aldosterone by the adrenal cortex (Llaurado, 1955). It is conceivable that the mobilization of water from the cells in response to an increased insensible water loss is followed by a shift of potassium from cells to extracellular fluid, and that this tendency of extracellular potassium concentration to rise stimulates the increased secretions of aldosterone as much as does the cessation of sodium intake (Laragh and Stoerk, 1955).

Clinical Applications. Good post-operative treatment is designed to promote the recovery of the patient from injury. It is important therefore to examine our present knowledge of the effects of injury to see if there is any way in which the normal response of the body to injury can be helped or beneficially modified. This response appears to be controlled by adrenal cortical hormones, the production of which in turn is probably mediated by the hypophysis and above this by centres in the hypothalamus; there is no evidence that hormone production is deficient or that the normal response is potentiated by the administration of adrenal cortical or corticotrophic hormone. If the hormonic basis of the response to injury cannot be beneficially modified, it seems unlikely that any of the other hormone dependent facets of the normal response are likely to be individually modified. Prevention of starvation may somewhat reduce the total loss of nitrogen by avoiding that fraction due to inadequate calorie intake. It is possible to reduce the ultimate loss of nitrogen only if sufficient non-protein calories can be supplied at the same time as fat, alcohol or fructose; this involves some additional risk of complications such as thrombophlebitis and extra discomfort is associated with prolonged intravenous infusions. The intravenous administration of protein supplements is seldom accompanied by the provision of large enough supplies of non-protein calories to prevent wastage by deamination of the protein or its component peptides or amino-acids. The human body seldom seems to make good use of such protein during the post-operative catabolic phase and amino-acid infusions are then commonly followed by an equivalent increase in nitrogen excretion.

changes in urinary composition subside. The body then passes into a state of "anabolism" during which enough nitrogen, potassium, sulphur, and phosphorus, as well as some sodium and chloride, are retained to enable the previously catabolized tissues to be reformed. This "anabolic" phase or period is the time of convalescence and may last many weeks. The successful restoration of lost tissue depends on the consumption of a good mixed diet containing sufficient calories and protein to supply the needs of anabolism, as well as of the ordinary daily requirements of energy and protein. The intensity of the "catabolic" phase and the quantity of protein tissue destroyed depend partly on the magnitude of the tissue injury; but both also depend on the initial state of nutrition of the individual patient. The maximum response follows severe injury in a heavily muscled healthy young male; a similar injury is followed by much less loss of tissue and a far smaller increase in urinary nitrogen excretion in a malnourished person whose total protein content has been reduced by disease or partial starvation before operation. On the other hand, the healthy patient shows some loss of tissue and of weight and a small increase in urinary nitrogen excretion after even small surgical injuries.

Changes in the Composition of the Blood. In spite of the large shifts of fluid, the extensive destruction of protein tissue and the close renal conservation of sodium and water, there is little alteration in the composition of the blood. An initial increase in packed cell volume (hæmoconcentration) which varies with the water intake and is most marked after burning, is followed by a sharp fall (hæmodilution) accompanied by reduction in plasma protein concentration affecting mainly and most lastingly the albumin fraction. The globulin concentration rises to normal or above within a few days, but albumin concentration may remain depressed for 2 or 3 weeks or longer. This prolonged depression of plasma albumin is not due entirely to dilution, but appears to be related to the state of protein nutrition of the subject. There is much evidence which indicates that there is a close quantitative relationship between tissue protein and plasma albumin, 1 g. of albumin being in equilibrium with about 30 g. of tissue protein. The reduction in plasma albumin concentration after injury or operation may be, as in starvation, another indication of the loss of tissue protein. Other changes in blood composition are inconstant; plasma sodium may fall a little, potassium concentration seldom changes when renal function is satisfactory, but urea may rise during the first day or two.

Loss of weight after severe accidental or surgical injury may amount to 10 per cent or more of the initial weight. This loss of weight is due to a combination of insensible water loss, excretion of urine and the catabolism of protein and fat. It is offset by the administration of water and especially of saline, part of which is retained in the body. When large quantities of fluid containing sodium salts are administered, the measurable loss of weight may not appear until 5 or 6 days after operation, but the eventual loss of weight will be as great as if fluid had not been given, although the lowest post-operative weight may not be reached until the eighth or tenth day, instead of on the third or fourth day. The amount of weight lost depends on the state of nutrition and perhaps also on the water and mineral content of the body at the time of injury. Insensible water loss is increased by up to 50 per cent after major operations This increased requirement together with the continued excretion of urine and the restriction of fluid intake may result in the loss of 2·6 Kg. (5·72 lb.) of body weight in the first 24 hours after operation (Wilkinson, 1956). Behind the large increase of insensible water loss after injury lies an unexplained and

quantities of sodium, potassium, and other cations, and of chloride, bicarbonate and other anions, in a suitable concentration in the body fluids which surround the cells and form part of the substance of the cells. This normal composition of the cells and their environmental fluid is subject to repeated disturbances following the ingestion of food and drink, and as the result of normal metabolism, the production of intestinal secretions, urine and insensible water loss. These daily changes are resisted by a complex system of buffer substances. In the plasma the bicarbonate-carbon dioxide system, the sodium phosphate-sodium dihydrogen phosphate system and the plasma proteins, in addition to the potassium phosphate and hæmoglobin systems of the red corpuscles, impose the primary limitations on changes in pH.

The tension of carbon dioxide in the alveolar air is the factor on which the carbonic acid concentration of extracellular fluid depends. This concentration is normally 1·25–1·35 mEq. per litre. The concentration of bicarbonate ion in extracellular fluid is dependent on the total quantity of cations, the "alkali reserve," available for combination or equilibrium with it; this quantity (the so-called total available "base") is indicated by the amount by which the sum of the extracellular (or plasma) cations (sodium, potassium, magnesium, and calcium) exceeds the sum of the anions (chloride, phosphate, sulphate, keto acids, and plasma proteins). This difference is equal to the quantity of carbonic acid which must react with cation to form bicarbonate in order to maintain the neutrality of reaction of the blood; this quantity of carbonic acid, or the "carbon dioxide combining power," is normally 25–27 mEq. per litre. The pH of the extracellular fluid is determined by the relationship between the concentration of carbonic acid and bicarbonate, and is held with remarkable constancy at 7·4 under most circumstances. It is obvious that reduction in the total quantity of available cations may occur, for example by the loss of a large quantity of sodium in excess of any loss of anions in intestinal fluids lost by vomiting or diarrhœa, and that without compensation this will tend to cause the reduction of the alkali reserve and hence of extracellular bicarbonate and thus a shift of pH. Similarly an increase in anion content without any alteration in cation content would reduce the cations available to balance bicarbonate and cause its concentration to fall and also lead to a tendency to a fall in pH. The reduction of "alkali reserve" in such circumstances is associated with a relative excess of carbon dioxide as carbonic acid over bicarbonate in the extracellular fluid.

The main factor in limiting the rise of hydrogen ion concentration consequent on the accumulation of the acid products of metabolism is excretion of hydrogen ion by the renal tubules, as well as the elimination of inorganic acid radicles such as sulphate chloride and phosphate and organic radicles such as pyruvate and lactate. In addition, the control of the excretion of cations such as potassium and sodium by the renal tubules, and hence of the body content of these ions, is the factor which determines the quantity of cations in the body in excess of anions which is available to form bicarbonate, the so-called alkali reserve. When the pH of the body fluids has been disturbed the normal state is regained only when the excess of hydrogen ion has been excreted by the kidneys; until that is achieved the united efforts of the buffering systems is able only to limit the degree of disturbance.

There are several reasons therefore why the kidneys play such an important part in the regulation of the composition of the internal equilibrium of the body. They excrete anion when this is in excess and conserve cation such as sodium when this is deficient.

The large urinary loss of potassium which is a normal feature during the first 2 or 3 days after injury, is well tolerated by fit well nourished patients; it is not an indication for the administration of potassium salts. On the contrary, the transfer of potassium from intracellular to extracellular fluid during the first 48 hours after injury clearly indicates that infusions of potassium salts during this period are not only unlikely to be of any value, but may be dangerous and ill-advised. A small volume of urine containing much potassium and little sodium is a normal sequel to major surgical operations and severe accidental injury, and does not call for large rectal or intravenous infusions of saline, glucose solution or tap water in an attempt to induce a wholly unnatural diuresis. Renal conservation prevents any large loss of sodium in the urine, and if large volumes of gastro-intestinal secretions are not lost by gastric aspiration, diarrhœa or fistula there is seldom any need to administer sodium salts during the first week after operation.

During the first 2 or 3 days after severe injury, intense thirst is experienced by most patients. This thirst is related in time to the period of potassium diuresis and to the period of greatly enhanced insensible water loss. Little relief is obtained by even abundant drinking which is frequently followed by copious vomiting; the intravenous administration of glucose solution or 0·9 per cent saline does not relieve and usually prolongs this thirst. It is probably associated with intracellular dehydration and hypertonicity, and passes off towards the end of the potassium diuresis. It is best relieved by frequent washing of the mouth with ice cold water.

The recovery of a patient from even major operations is commonly uneventful provided that abnormal fluid losses can be avoided and the consumption of food is allowed and encouraged as soon as appetite returns. The parenteral administration of fluid, glucose, or protein is seldom required. After injury, human beings, like other animals, can tolerate a short period of starvation for water as well as for food during which the body derives its energy, water, and protein requirements from its own tissues. If excessive bleeding is avoided or adequately replaced by transfusion and infection is prevented, survival depends on the possession at the time of injury of sufficient bodily resources and the hormonic means of using them to live and to heal.

ACID-BASE BALANCE

A detailed description of all the mechanisms which determine the control of hydrogen ion concentration in the body is beyond the scope of this account. Some understanding of the normal regulation and of the possible modes of disturbance of hydrogen ion concentration are however essential for the treatment of the rare clinical examples which the surgeon may encounter. The difficulty which many clinicians experience in understanding the processes involved in this regulation is exaggerated by the confusion in terminology which results from the conventional clinical use of the term acid and base; in this convention "acid" is applied to the anions such as bicarbonate and chloride, and "base" to the cations such as sodium and potassium and also hydrogen ion. Without completely revising the current conception of so-called acid-base balance it is impossible to change the current use of these terms and in this account such revision seems out of place.

The maintenance of chemical equilibrium in the body depends on the preservation of hydrogen ion concentration within narrow limits, and at the same time of the total

quantities of sodium, potassium, and other cations, and of chloride, bicarbonate and other anions, in a suitable concentration in the body fluids which surround the cells and form part of the substance of the cells. This normal composition of the cells and their environmental fluid is subject to repeated disturbances following the ingestion of food and drink, and as the result of normal metabolism, the production of intestinal secretions, urine and insensible water loss. These daily changes are resisted by a complex system of buffer substances. In the plasma the bicarbonate-carbon dioxide system, the sodium phosphate-sodium dihydrogen phosphate system and the plasma proteins, in addition to the potassium phosphate and hæmoglobin systems of the red corpuscles, impose the primary limitations on changes in pH.

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So efficient is the renal regulation of body composition that disturbances of pH seldom occur unless renal function is impaired, and are most often due to marked alteration of respiratory functions. Sodium, the predominant cation of extracellular fluid, is conserved by the kidney in three ways: by absorption of sodium with bicarbonate from tubular urine, by the exchange of sodium in the tubular urine for hydrogen ion which is then excreted in the urine in combination with urinary buffer salts, and by the exchange of ammonium ion for the sodium ion in the tubular urine. These processes have the common purpose of conserving sodium and some bicarbonate, and share in various ways the common mechanism of sodium ion-hydrogen ion exchange. By these means almost the whole of the bicarbonate of the glomerular filtrate is reabsorbed and urine can be formed which at a pH of 4·4 is nearly a thousand times as acid as the glomerular filtrate from which it originates.

Unless some of the strong acids such as hydrochloric and sulphuric formed in the renal tubules by hydrogen ion exchange could be excreted as weaker salts the limiting pH of the urine would be too readily reached; the capacity for excretion of such acids is increased by their combination with ammonia, formed in the tubular cells from glutamine and other amino-acids. This ammonia as ammonium carbonate diffuses into the tubular urine and replaces sodium in the salts of strong acids, the resulting sodium bicarbonate being reabsorbed by the tubular cells and conserved. These processes fail when an excessive quantity of acid is produced, for example in diabetic ketosis, which exceeds the capacity of the various tubular mechanisms; there is then a loss of sodium as well as an increase in the acid content of the body. Damage or disease of the tubular cells may reduce the capacity of the compensatory processes and also lead to accumulation of acid.

Acidosis and Alkalosis

These two terms indicate changes in hydrogen ion concentration in extracellular fluid. Acidosis indicates an increase in hydrogen ion concentration, a fall in pH, but not necessarily more anion or "acid" in the extracellular fluid. In alkalosis there is decreased hydrogen ion concentration and pH rises, but there is not necessarily an increase in the quantity of cation or "base." There are many clinical situations in which both cations and anions are lost, the proportions of each varying according to the kind of fluid which is lost. Such complicated alterations in the composition of the extracellular fluid may result from the loss of gastro-intestinal secretions and other body fluids. In trying to make a diagnosis it is always important to remember that when the extracellular ionic concentrations are abnormal, distortion of body composition may be far advanced, but that when total extracellular fluid volume is reduced changes in concentration appear larger than they really are in terms of the total content of the ions concerned. For clinical purposes alkalosis and acidosis are classified as "metabolic" or "respiratory" in type. Confusion has been increased by the description of "compensated" alkalosis or acidosis which is said to exist when the various mechanisms which were earlier mentioned as regulating pH are able to resist the tendency to alteration in pH. When such compensation fails some clinicians apply the terms "acidæmia" and "alkalæmia" to the resulting pH changes but in the present account these are described as acidosis and alkalosis.

Metabolic Acidosis. This is the common clinical type of acidosis. The change in pH is due to the reduction in extracellular bicarbonate concentration secondary to the

accumulation of other anions, for example in diabetic acidosis, of lactic and keto acids of metabolic origin, or in renal failure because of impaired excretions of phosphate and sulphate. Metabolic acidosis may also result from the loss of both cations and anions when the cation loss exceeds that of anions; it is then essential that the bicarbonate be reduced in order to restore chemical equilibrium between the total cation and total anion. The displaced bicarbonate is converted into carbonic acid and when carbon dioxide is excreted by the lungs the freed hydrogen ion tends to disturb the extracellular pH. The ingestion of an excess of anions as ammonium or calcium chloride, or the excessive production of organic acids in violent exercise, in fever or infectious diseases also causes the temporary replacement of bicarbonate and the tendency to acidosis. To compensate for metabolic acidosis renal hydrogen ion excretion is augmented, and conservation of sodium and bicarbonate ions is increased. At the same time the rising extracellular hydrogen ion concentration stimulates the respiratory centre and more carbon dioxide is excreted in the lungs and the extracellular carbonic acid concentration falls, returning the ratio of bicarbonate to carbonic acid and thus of pH to normal, although the total quantity of bicarbonate remains low.

CLINICAL FEATURES. The most obvious feature of severe acidosis is the deep harsh respiration or "air hunger" which is typically found in association with marked depression of plasma bicarbonate concentration and reduction in pH. In addition to the marked increase in the depth of respiration the rate is increased to as much as 50 or more excursions per minute. The pulse rate and systolic and diastolic blood pressures also are raised.

DIAGNOSIS. The diagnosis of acidosis of moderate degree depends firstly on the history of the patient's illness, and in surgical patients loss of gastrointestinal secretion is much the most common cause of acidosis. By measurement of the plasma bicarbonate concentration and pH the suspicions aroused by the history may be confirmed and the severity of the disturbance may be judged. In addition measurement of the hæmatocrit and plasma sodium, potassium, and chloride concentrations often provides valuable additional assistance in designing suitable treatment. In severe acidosis the patient may be comatose and this combined with the stertorous respirations and any history that can be obtained, is often enough evidence on which to begin treatment.

TREATMENT. This depends mainly on relieving the cause if possible and in assisting the various compensating processes. The type most susceptible to treatment is that due to loss of intestinal secretions with large losses of sodium and water; here the administration of solutions such as Darrow's, which contains some potassium chloride as well as sodium lactate, is indicated when the diminished extracellular fluid volume has been first increased by the rapid infusion of 0 9 per cent saline. The extracellular content of bicarbonate can be increased by the administration of 500–100 ml. of a 1·86 per cent solution of sodium lactate over a period of 4–6 hours, but in practice this does not usually seem to possess any special advantage over isotonic saline. Acidosis due to renal failure does not respond well to sodium lactate or to any other form of treatment and potassium salts should not be used in this kind of disturbance. Some short lived improvement in the acidosis of severe infection may follow the administration of sodium lactate.

Respiratory Acidosis. Acidosis due to interference with normal gas exchange in the lungs, with retention of carbon dioxide and an increase in carbonic acid and hence of extracellular hydrogen ion concentration, is less common than metabolic acidosis. It

may be due to depression of the respiratory centre by injury, by poisoning with barbiturate, morphine, or alcohol. Poor pulmonary ventilation due to emphysema, pulmonary œdema, bronchopneumonia, in association with congestive cardiac failure, or during anæsthesia especially when muscle relaxants are employed, or in patients with paralysis of the respiratory muscles due for example to poliomyelitis, also diminishes carbon dioxide excretion.

CLINICAL FEATURES. The character of the respirations are the most obvious sign of respiratory as well as of metabolic acidosis and the underlying cause is usually also sufficiently evident.

TREATMENT is unsatisfactory unless the primary cause can be relieved.

Metabolic Alkalosis. In this state the hydrogen ion concentration is reduced and the extracellular bicarbonate ion concentration (carbon dioxide combining power) is raised. This may be due to an increase in bicarbonate to compensate for loss of anions such as chloride. The raised bicarbonate causes an alteration in the carbonic acid-bicarbonate ratio and a rise in pH. This inhibits the respiratory centre and carbon dioxide retention results from the diminished pulmonary exchange, the extracellular carbonic acid rises and tends to reduce pH to within normal range. The commonest form of this disturbance in surgical patients occurs following repeated vomiting in pyloric stenosis or prolonged gastric aspiration; both these processes lead to larger losses of chloride than of sodium or potassium and to a compensatory increase in extracellular bicarbonate. When the loss of gastric secretion is short-lived the loss of chloride predominates, but in prolonged losses the need to replace sodium and water by the infusion of saline in order to maintain extracellular fluid volume results in correction of the loss of sodium and chloride but not that of potassium. The content of chloride and sodium in the lost gastric juice tends to decline after repeated losses, but potassium content does not fall and in achlorhydria may even increase a little because of the large quantities of gastric mucus, with a high potassium content, which may be lost. Such a repeated loss of potassium combined with a restricted intake because of partial starvation, and the continued daily loss of potassium in the urine, leads after 2 or 3 weeks to considerable reduction in the body content of potassium. As has been pointed out earlier, there is no way of preventing the continued loss of potassium in the urine which may be increased by the need to transfer water from the cells when water intake also is inadequate. Cooke *et al.* (1952) found that up to 50 per cent of the potassium lost from the cells could be replaced, two-thirds by sodium and one-third by hydrogen ions, but this shift of hydrogen ion into the cells causes an intracellular acidosis and accentuates the extracellular alkalosis. These changes in cellular composition can be reversed only by the administration of sufficient potassium, preferably as potassium chloride. This potassium is transferred into the cells and displaces sodium and hydrogen ions thus correcting the intracellular acidosis. When the sodium and hydrogen ions are returned to the extracellular fluid they reduce the extracellular alkalosis. Metabolic alkalosis should be suspected in any circumstances in which there is potassium depletion.

Alkalosis with potassium deficiency also follows the prolonged administration of desoxycorticosterone acetate and sometimes A C.T.H. or cortisone, it may be found in patients with some forms of Cushing's syndrome and certain kinds of adrenal cortical neoplasm, after the prolonged intravenous infusion of saline and in some rare renal tubular disturbances.

CLINICAL FEATURES. A mild degree of alkalosis does not have any characteristic feature except an increase in plasma bicarbonate concentration. In severe alkalosis the most striking disturbance is the phasic respiration; a period of apnœa is followed by a few shallow breaths which gradually deepen and then become shallow and decline to apnœa. The severity of the respiratory disturbance is related to that of the pH. There may be tetany in severe alkalosis due to the changed pH altering the proportion of ionized to unionized calcium in the extracellular fluid.

TREATMENT. Apart from trying to relieve the primary cause of the disturbance the most important objective is to overcome the very large potassium deficit which always underlies severe alkalosis in surgical patients. The replacement of potassium by the administration of potassium chloride is the most important aspect of treatment. The widely advocated employment of ammonium chloride is futile; this recommendation is based on the idea that the chloride loss in the vomitus is of major therapeutic importance and ignores the large loss of potassium which may amount to a third or more (1000 mEq.) of the total initial body content. Ammonium chloride does nothing to reverse the transfer of sodium and hydrogen ions into the cells and provides only a theoretically metabolizable cation ammonium, and an excess of anion as chloride. When there are associated losses of sodium and water these too should receive due attention, but the main emphasis in most examples of metabolic alkalosis must be placed on the replenishment of the body content of potassium. The intravenous infusion of solutions of potassium salts are usually needed only in the initial part of this treatment, the bulk of the potassium should be taken by mouth and the consumption of ordinary food should be resumed as soon as possible.

Respiratory Alkalosis. In this type of alkalosis there is a reduction in extracellular carbonic acid because of hyperventilation, the carbonic acid-bicarbonate relationship is disturbed and pH rises. Although at a raised pH the affinity of hæmoglobin is increased and oxygen saturation is normal, the dissociation of oxyhæmoglobin is reduced and tissue oxygen uptake may decline. In surgical patients this state is probably most common during anæsthesia as a transient accompaniment of vigorous manual pulmonary ventilation in the use of the muscle relaxing agents. It also occurs because of hyperventilation in men working in very hot dry environments, in high fever, at high altitudes and in severe salicylate poisoning especially in children.

THE EFFECTS OF ASSOCIATED DISEASES

Modern anæsthesia has reduced the hazards formerly associated with major surgical operations on patients with severe disturbances of cardiac and pulmonary function, but these disabilities still retain their potentialities in producing post-operative complications after the acute dangers of the operation have been successfully surmounted. The recovery of the patient more than ever depends on the awareness of the clinician of the possible variations of response by the patient within the limits imposed by his cardiac and renal disease.

Hepatic Disease. Severe disturbances of water and sodium content and equilibrium are common in both acute and chronic liver disease, but it is uncertain exactly how these disturbances are caused. In acute liver disease oliguria or even anuria are not uncommon and delay in diuresis after drinking a large volume of water is well known. Indeed, the

increase in the volume of the 24 hour output of urine has long been recognized as perhaps the earliest sign of improvement in several kinds of liver disease. It has been suggested that the normal catabolism or inactivation of pituitary or adrenal cortical hormone by the liver may be impaired in severe disease and thus may lead to the retention of both water and sodium. In biliary obstruction, severe functional impairment of the liver may not occur for some time, especially in the absence of infection. In cirrhosis of the liver malnutrition commonly leads to reduction of the lean tissue mass and total body weight is often below the ideal weight for the individual in spite of the accumulation of ascites; the total content of sodium is increased and the distribution of body water is changed, the extracellular fluid volume being unusually high; total potassium content is however reduced by protein depletion and the reduction of lean tissue mass. The depression of total plasma protein affects albumin to a greater degree than globulin and this also may have an effect on body fluid equilibrium. The daily urinary sodium output is usually low in patients with chronic liver disease because of renal conservation of sodium. The balance which may be achieved by careful dietary restriction between sodium intake and output is precarious and readily disturbed by small variations in intake or output, the result of an increased sodium intake by intravenous infusion or of the response to even small operations or minor infections. The depletion of plasma albumin concentration in chronic liver disease is an expression of the general protein depletion which is common in these patients. Attempts to increase this concentration by the transfusion of concentrated human serum albumin are bound to fail because of the equilibrium which exists between total protein and the circulating plasma proteins. Much of the administered albumin is readily lost into ascitic fluid and elsewhere out of the circulating blood. The intravenous infusion of all kinds of fluids, but particularly of saline, is dangerous after operation on patients with damaged livers because of their loss of ability to respond to abnormal loads of water and also because of the excessive quantity of sodium in the body.

Cardiac Disease. Patients with congestive cardiac failure tend to retain both sodium and water to a greater degree than normal after operation and are therefore in greater danger of developing œdema. The use of intravenous infusions demands especial caution after operations of any kind in such patients, and must always be designed for the requirements of the individual and his particular circumstances rather than as the routine use of arbitrary therapy.

Renal Disease. The reserve functional capacity of the kidneys is so great that distortion of body composition arises only in advanced renal disease. The main effect of severe renal functional impairment is to reduce the adaptability of the individual and his capacity to respond adequately to the large disturbances of normal metabolism which follow severe injury or infection. In severe renal disease the loss or impairment of specific tubular function often requires that a larger volume of urine be formed to excrete adequately the same total quantity of solutes. The same impairment of tubular function results in less effective conservation of constituents of the glomerular filtrate in the larger final volume of urine, and thus in the loss from the body of components which, with normal tubular function, would be conserved. Sudden loads of water by causing diuresis may exaggerate such losses, for example of sodium.

The survival of a patient with advanced renal disease from a major surgical operation may depend on whether his residual renal function is sufficient to cope with the extra excretory burdens following the unavoidable post-operative metabolic disturbance.

Poor concentrating capacity prevents the production of a concentrated urine and an increased water intake is essential for the formation of sufficient urine to carry away the metabolic products; the coincident reduction in response to a sudden large intake of water by a rapid and complete diuresis increases the danger of administration of water in the form of glucose solution after operation. Attempts to compel diuresis by the administration of saline or sodium sulphate solution after operation are dangerous as well as ineffective, and in elderly patients impaired renal function makes even the intravenous infusion of glucose solution a serious risk. If any doubt exists of the patient's renal capacity, some attempt should be made before operation to find out how much renal reserve there is by such a simple test as the response to the ingestion of a pint of water; failure to produce and maintain a diuresis and a fall in specific gravity suggests that renal function may be impaired.

Anuria. The term anuria should be employed only when the output of urine from the kidneys has ceased. The term oliguria should be used in circumstances when the daily urine volume is less than 500 ml. per day. Anuria may be caused by primary renal disease such as acute nephritis or pyelonephritis or be due to the effects of poisons such as diethylene glycol or mercury. It may follow mechanical obstruction of the renal pelvis or ureter by stone, by sulphonamide crystals or by the inadvertent ligation of both ureters. It is commonest however, following mis-matched blood transfusion, concealed accidental hæmorrhage or abortion. There are two types of pathological lesions in the kidney (Oliver *et al.*, 1951) After poisoning there is usually necrosis of the cells lining of the proximal tubules, but the basement membrane is preserved and regeneration and return of function are possible. In the other type of lesion, the whole of the nephron is affected and the distribution of the lesion is widespread in the organ, but some nephrons escape except in massive cortical necrosis. There is a uniform pattern of renal functional disturbance. The clinical course can be divided into four stages (Bull *et al.*, 1950). In the stage of onset shock is severe and prolonged. During the next stage of anuria or oliguria, which may last for 3 weeks, renal blood flow is reduced to as little as 10–30 ml. per minute and less than 300 ml. of urine per day is secreted. Half the total deaths occur in this stage from cardiac arrest due to the accumulation in the extracellular fluid of potassium released from the cells. The accumulation of acid products of tissue metabolism causes acidosis with characteristic respiratory changes, and if sodium and water have inadvertently been administered there may be marked alteration in extracellular fluid volume.

The early diuretic stage follows in patients who recover, the daily urine volume increasing rapidly to reach a litre or more, but the urine remains an almost unmodified glomerular filtrate with a specific gravity of 1,010 or less. If large volumes of such fluid are lost, the extracellular fluid volume may decline. During this stage it is dangerous to administer excessive volumes of fluid in attempts to replace that lost by urine and to cover the theoretical extra-renal requirements, and care must be taken not to increase the severity of the diuresis inadvertently in this way. Only in the late diuretic stage does evidence of tubular function again appear, it can be recognized only by the chemical alterations in the urine and the decline in the daily output.

The history of the illness is as usual of primary importance in diagnosis and is often sufficient to give a clear indication of the likely cause, for example in abortion, accidental uterine hæmorrhage, mis-matched blood transfusion and poisoning. It is more difficult when oliguria after an operation is unusually prolonged and becomes more instead of

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intracellular potassium temporary reduction may follow the administration of 50 units of insulin and 50 g. of glucose, or the administration of calcium lactate. Potassium may be extracted from the body by perfusion of the blood through an artificial kidney, but this method involves great expense in the maintenance of apparatus and staff. The use of peritoneal dialysis or the perfusion of an isolated loop of intestine has met with little success. Potassium may be extracted from the extracellular fluid by the oral or rectal administration of suitable ion exchange resin. A sulphonic resin charged with sodium (Evans *et al.*, 1953) has considerable theoretical advantages in the anuric patient; resins charged with ammonium are liable to increase the blood urea concentration following the absorption of ammonium. Usually 15 g. of resin mixed with water or syrup is given three or four times a day. The uptake of potassium by the resin is related to the length and time the resin is in contact with the body fluids, and if this period is less than 12 hours little exchange occurs. Up to 75 mEq. of potassium may be extracted per day, just as much as is usually released during the early stages after operation or injury. Evans *et al.* recommended that the resin should be given as soon as the serum potassium concentration exceeds 6 mEq. per litre and continued until it falls below 5 mEq. per litre.

The recent improvement in the prognosis of anuric patients is undoubtedly related to the greater understanding of the pathology of this condition. Whereas formerly attempts to induce a diuresis by the infusion of solutions of glucose or sodium sulphate were often prolonged for days, it is now generally recognized that the careful restriction of the intake of water and minerals is essential if various forms of therapeutic intoxication are to be avoided. Fewer patients now die of pulmonary œdema or water intoxication. There is good reason to anticipate that the careful conservative management by restriction of the intake of water, protein, sodium, and potassium salts combined with the administration of 100 g. of glucose per day may do as much to promote the survival of the anuric patient as more complicated regimes. Timely use of a resin and an occasional purge may in addition delay the rise of the extracellular potassium concentration. Sulphonamide drugs should not be administered to anuric patients. Of the antibiotics, crystaline penicillin alone may safely be given in a daily dose. A single dose of the other antibiotics is usually sufficient to maintain an adequate concentration during the anuric stage. In the diuretic phase, the first requirement is for sufficient water to equal the daily urinary volume and the insensible water loss. It is essential that the urinary content of sodium and potassium be measured daily in order that the loss of these elements can be followed and their replacement accurately undertaken. In addition, it is a wise precaution to measure daily the serum concentrations of sodium, potassium, and chloride. Apart from the consumption of an adequate mixed diet, it may be necessary to add potassium in the form of fruit, fruit drinks, and if the serum concentration falls, as potassium chloride tablets.

LOSS OF GASTROINTESTINAL SECRETIONS

Gastrointestinal secretions may be lost by vomiting or gastric aspiration, diarrhœa or from fistulas. The effects of such losses are closely related to their rate and volume. These secretions are primarily derived from extracellular fluid and when losses are large and rapid they lead to acute reduction of the volume of extracellular fluid; compensation for such reduction, by the transference of water from intracellular fluid or of sodium from the bones, takes time and so is unable to prevent the reduction of plasma and extracellular

less severe. In these circumstances the diagnosis of tubular necrosis may be delayed for several days. After operations, oliguria is normal in the absence of an artificial high intake of water, but is associated with a concentrated urine of specific gravity 1,026 to 1,036 and a low or falling content of sodium, and at least for 48 hours after injury a high potassium content. Tubules which are able to conserve sodium and excrete potassium in high concentration in small volumes of urine may not be damaged. When however, only small volumes of urine of specific gravity below 1,010 are passed, and if in addition the sodium content is high and that of potassium is low, the unmodified state of the urine indicates severe impairment of tubular function.

When renal function is severely impaired, the accumulation of water in the body is indicated by hæmodilution and a falling plasma sodium concentration. Elevation of the blood urea and plasma potassium concentrations indicate the accumulation of the products of protein catabolism. In such circumstances, the plasma potassium concentration ought to be measured at least daily, for during the anuric stage, accumulation of potassium in the extracellular fluid is inevitable and the concentration may reach a toxic level.

Treatment. In many cases tubular epithelium will eventually regenerate if the patient survives sufficiently long. Any renal ischæmia due to circulatory disturbance should be corrected as rapidly as possible. Until glomerular filtration is re-established nothing can be excreted by the kidneys, and if water and minerals are administered in excess of the quantities lost by insensible loss through the skin and expired air, and in the sweat, fæces or vomitus, the excess will accumulate in the body. In anuria diuretic agents are useless and decapsulation of the kidneys, or spinal or splanchnic block are ineffective. The daily intake of water should not exceed the 1,000 ml. in adults which is sufficient to supply the water for extra-renal loss. Since sodium and potassium are lost only by vomiting, in the stools or by sweating, the intake must be stopped. Acidosis and alkalosis cannot be corrected during anuria, but do not appear to cause much harm. The work of Gamble (1947) has shown that in the starving normal person, the daily provision of 100 g. of glucose will reduce the catabolism of protein to the minimum of about 40 g. per day. In the starving anuric patient, there is no evidence that the provision of more than 100 g. of glucose confers any metabolic benefit, and there does not seem to be much justification for the administration of large quantities of carbohydrate and fat to the anuric patient. It is essential however, that the intake of any form of protein should be stopped in order to prevent unnecessary accumulation of potassium and urea. The slow intravenous infusion of 50 per cent glucose solution through a polythene catheter into one of the great veins has been recommended but this procedure is accompanied by an appreciable risk.

It is important to recognize that in patients who have severe injuries involving much damage to muscle, protein catabolism both in the damaged tissue and elsewhere in the body is inevitable, with the associated release of protein residues and potassium into the extracellular fluid; a similar inevitable release of potassium must occur in patients during involution of the uterus after abortion or intra-uterine hæmorrhage. The catabolism of tissue protein might result in the release of from 6–30 g. of nitrogen per day in the first week after injury. With each gram of tissue protein nitrogen 2–3 mEq. of potassium also may be released so that from 12–60 mEq. of potassium may reach the extracellular fluid every day. When the extracellular potassium concentration rises because of the release of

treatment by saline infusion. The potassium losses become important only when they continue for a sufficient length of time in association with a varying degree of starvation and the continued daily loss of potassium in the urine. Progressive depletion of the intracellular content of potassium is followed by the transfer of sodium and hydrogen ions into the intracellular fluid with a consequent intracellular acidosis. How much of the functional disturbance of advanced potassium depletion is due to loss of potassium and how much to the gain in sodium and hydrogen ion content of intracellular fluid is uncertain.

There is seldom any change in the chemical composition of the extracellular fluid until vomiting has led to very large losses of body fluid. The first indications are usually an increase in carbon dioxide combining power and a decrease in chloride concentrations; until a late stage the concentration of sodium is maintained by renal conservation and by the transfer of sodium from bone, and that of potassium by the transfer of potassium from cells because of tissue catabolism resulting from partial starvation and because of intracellular dehydration following the reduction in effective water intake. Finally however, there is marked elevation of the carbon dioxide combining power and plasma chloride concentration is much reduced; plasma sodium concentration varies considerably and may be raised when water depletion is unusually great or lowered following the intravenous infusion of glucose solution. Potassium concentration while sometimes below normal may be elevated by hæmoconcentration or when renal function is impaired.

Treatment. Since the losses of body constituents vary with the duration of vomiting and the degree of the accompanying starvation, treatment also must be varied. Acute losses of gastric juice over a short period of a few hours produce acute reduction in extracellular fluid volume which can be satisfactorily corrected by the rapid intravenous infusion of sufficient 0 9 per cent saline; subsequently the kidneys adjust the disproportion in the quantities of sodium, chloride and water which are thus administered. When vomiting has continued long enough to cause only a moderate degree of potassium depletion and extracellular alkalosis it is still possible safely to restore the extracellular fluid volume by the rapid infusion of 0·9 per cent saline and then, provided the cause of the vomiting can be relieved surgically, to delay the replacement of potassium and the full correction of extracellular alkalosis until after operation. When vomiting has continued for more than a week there is always some degree of potassium deficiency as well as alkalosis. The importance of the finding of a severe extracellular alkalosis is that it is an indication of the severity and long duration of the losses of gastric secretions, and indirectly of the large loss of potassium with which such losses are associated; a carbon dioxide combining power of more than 85 volumes per 100 ml. should always lead to the suspicion that there has been severe depletion of potassium. In such patients, no matter what may be done about restoring extracellular fluid volume, the early administration of a large quantity of potassium chloride is also essential. It is worth trying first the consumption of as normal a diet as possible combined with gastric lavage night and morning, and the oral administration of up to 12 g. potassium chloride per day. If food cannot be tolerated or [illegible]

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Those surgeons who deny that a jejunostomy is ever necessary for the resuscitation of patients with pyloric stenosis and who believe that gastro-jejunostomy is always equally

fluid volume and the onset of oligæmia. The fluid lost usually consists of mixed secretions from more than one region, and the composition of the individual secretions also may vary widely from one patient to another and in any one patient at different times. Median normal values for the chief components of gastrointestinal secretions are shown in Table 4. In general however, the continued loss of gastric secretion leads to the loss of chloride, and smaller losses of sodium and potassium, with compensatory alkalosis. The fluid lost in diarrhœa and from intestinal fistulas contains more sodium than chloride and is followed by compensatory acidosis in addition to the reduction in extracellular fluid volume. Although the predominant effect of the loss of gastrointestinal secretions is a reduction in sodium and water content of the body, when such losses continue for several days the loss of potassium becomes clinically important. Because of their more obvious effects on the plasma volume the sodium and water losses are usually readily recognized and replaced by the intravenous infusion of saline, but the smaller losses of potassium from the alimentary tract, the continuing loss of potassium in the urine and the reduction of potassium intake are less often recognized and over the course of a week or more may together amount to several hundred milliequivalents.

Œsophageal Obstruction. Œsophageal obstruction although seldom complete has usually continued for a long time before the patient reaches the surgeon and has been sufficiently severe to cause partial starvation. Such patients have been supplying an increasing proportion of their daily needs for continuing metabolism from their own tissues. This leads to the loss of fat and lean tissue with reduction of the total body contents of nitrogen and potassium; there is however a relative increase in sodium content with a disproportionately large extracellular fluid volume. When œsophageal obstruction is complete, in addition to starvation salivary secretions of up to 1,500 ml. per day are lost. Such patients have a poor tolerance for intravenous infusions. Before operation, if dilatation of the œsophageal stricture and oral feeding are impossible their general condition is best improved by feeding through a jejunostomy. The improvement which results from 2 to 3 weeks feeding of a fortified milk mixture of high caloric and protein content well justifies the delay in operation. Ileus is common after resection of the œsophagus and has been attributed to division of the vagus nerves but potassium deficiency may also be an important factor. Prolonged gastric aspiration is sometimes necessary after operation, and it is difficult and sometimes impossible to replace the resulting large losses of fluid. The need for intravenous replacement can usually be almost entirely avoided by returning the fluid aspirated from the stomach to the intestine through a jejunostomy and in addition by jejunostomy feeding the duration of post-operative starvation can be reduced.

Loss of Gastric Secretions. The proportions of sodium, potassium, and chloride lost in gastric juice vary considerably; at least in the early stages of repeated vomiting the loss of chloride predominates and this leads to compensatory alkalosis in the extracellular fluid. The kidneys respond to the loss of sodium by conserving it closely and the urine becomes and remains acid until the sodium losses are replaced. The extracellular fluid depletion which results from repeated vomiting is usually treated by the intravenous infusion of 0 9 per cent saline. This replaces satisfactorily the chloride and water losses but supplies an excess of sodium (153 mEq per litre, gastric juice contains average of 50 mEq. per litre) and does nothing to correct the smaller loss of potassium. The reappearance of chloride in the urine is not a reliable indication of the adequacy of

treatment by saline infusion. The potassium losses become important only when they continue for a sufficient length of time in association with a varying degree of starvation and the continued daily loss of potassium in the urine. Progressive depletion of the intracellular content of potassium is followed by the transfer of sodium and hydrogen ions into the intracellular fluid with a consequent intracellular acidosis. How much of the functional disturbance of advanced potassium depletion is due to loss of potassium and how much to the gain in sodium and hydrogen ion content of intracellular fluid is uncertain.

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TREATMENT. Since the losses of body constituents vary with the duration of vomiting and the degree of the accompanying starvation, treatment also must be varied. Acute losses of gastric juice over a short period of a few hours produce acute reduction in extracellular fluid volume which can be satisfactorily corrected by the rapid intravenous infusion of sufficient 0·9 per cent saline; subsequently the kidneys adjust the disproportion in the quantities of sodium, chloride and water which are thus administered. When vomiting has continued long enough to cause only a moderate degree of potassium depletion and extracellular alkalosis it is still possible safely to restore the extracellular fluid volume by the rapid infusion of 0·9 per cent saline and then, provided the cause of the vomiting can be relieved surgically, to delay the replacement of potassium and the full correction of extracellular alkalosis until after operation. When vomiting has continued for more than a week there is always some degree of potassium deficiency as well as alkalosis. The importance of the finding of a severe extracellular alkalosis is that it is an indication of the severity and long duration of the losses of gastric secretions, and indirectly of the large loss of potassium with which such losses are associated; a carbon dioxide combining power of more than 85 volumes per 100 ml. should always lead to the suspicion that there has been severe depletion of potassium. In such patients, no matter what may be done about restoring extracellular fluid volume, the early administration of a large quantity of potassium chloride is also essential. It is worth trying first the consumption of as normal a diet as possible combined with gastric lavage night and morning, and the oral administration of up to 12 g. potassium chloride per day. If food cannot be tolerated or vomiting continues or increases, the most certain means of relief both of the potassium deficiency and of the starvation is by feeding the patient through a jejunostomy. Those surgeons who deny that a jejunostomy is ever necessary for the resuscitation of patients with pyloric stenosis and who believe that gastro-jejunostomy is always equally

safe and satisfactory have perhaps been unusually fortunate in not having encountered patients with advanced potassium depletion.

The intravenous administration of ammonium chloride has been advised as a means of correcting the alkalosis due to prolonged vomiting since it provides chloride with a cation which is "disposable" in that the ammonium ion can be converted to urea or excreted unchanged in the urine. Such use of ammonium chloride lays the therapeutic emphasis on the wrong if the more obvious disturbance of alkalosis, rather than on the potassium deficiency which when severe, is the more important cause of illness, complications and death. When first encountered the patient may be very drowsy or even in coma; in such cases the intravenous replacement of potassium is necessary. A urinary output at the rate of at least 480 ml. per day or 20 ml. per hour should first be ensured by the intravenous infusion of 500 ml. of 5 per cent glucose solution. Thereafter up to 2 g. (26 mEq.) of potassium chloride (400 ml. of 0·55 per cent potassium chloride in 2·5 per cent glucose solution) may be administered over a period of 4 or 5 hours and up to 12 g. may be given during the first 24 hours. Usually only a small quantity of potassium is required to produce a marked improvement in the general condition of such patients and as soon as possible oral administration should be substituted.

After operations on the stomach or duodenum, it is occasionally necessary to continue gastric aspiration and to restrict drinking for several days because of delay in the return of normal gastrointestinal motility; this complication may persist for more than a week. Sometimes if both gastric aspiration and drinking are stopped motility returns, but rarely even this is not followed by improvement. When fear of an organic obstruction then leads to the abdomen being reopened the stoma is usually found to be wide-open and stiff with œdema and the gastric contents are swilled across it with each respiratory excursion. The cause of this complication remains uncertain but it seems to be more common in patients with prolonged severe pyloric stenosis with overt potassium deficiency. Further surgical measures except a jejunostomy are of little value, but a jejunostomy has the advantage that all aspirated fluid can be returned forthwith to the intestine, a full daily intake of calories, minerals, and protein can be resumed and intravenous infusion is no longer necessary. The stomach tube should always be removed as soon as the aspirated fluid smells wholesome and is not thickly turbid.

Duodenal Fistula. This is most common after difficult operations for duodenal ulcer when there is leakage from the closed duodenal stump or following the disruption of a gastroduodenal anastomosis; it may also occur following pancreatectomy. The fluid lost is a mixture of duodenal and pancreatic secretions and bile and is alkaline; usually sodium losses are marked and up to 2 or 3 litres of fluid may be lost in 24 hours leading to the rapid reduction of extracellular fluid and plasma volumes, hæmoconcentration, and acidosis. The volume of the daily loss usually declines with the reduction in extracellular fluid volume and increases again following the rapid administration of 0·9 per cent saline. Food and bile-stained fluid gush from the fistula a short time after eating and digestion of the surrounding skin causes severe pain. Although many duodenal fistulas close spontaneously within 7–14 days some persist and lead to repeated reductions of extracellular fluid volume. The difficulty of repeatedly replacing the lost fluid by intravenous infusions mainly arises from the differences in composition between the lost fluid and that employed for its replacement, commonly simply 0·9 per cent saline. The easiest way of avoiding this difficulty is by establishing a jejunostomy through which the collected fluid

discharged from the fistula is restored to the intestine together with a suitable feeding mixture of high protein and caloric content. The natural hesitation on the part of the surgeon to inflict another operative procedure and to create another fistula should not be allowed to delay too long the institution of a jejunostomy with its unrivalled opportunity of ready replacement and control of the fistulous losses.

Biliary Fistula. A biliary fistula is most common after operation on the gall bladder and bile ducts, but may also rarely follow an apparently easy and uneventful partial gastrectomy. When all the daily output of hepatic bile, amounting to 500 or 600 ml., is lost it is nearly equivalent to the daily loss of a similar quantity of extracellular fluid, since a litre of bile may contain from 100 to 150 mEq. of sodium. After about a week such repeated large losses of bile lead to the typical picture of sodium and water depletion and may be corrected by the rapid infusion of a sufficient volume of 0·9 per cent saline. The appearance of a biliary fistula is usually preceded by a rise in body temperature, malaise, and jaundice. The severity of the jaundice and the extent of the associated biliary peritonitis usually depend on whether a drain is still in position and the ease with which the bile first finds a way to the surface. Operative intervention is seldom required to close biliary fistulas which almost invariably close spontaneously if the bile ducts are not obstructed. It is important not to allow large losses of bile consequent on deliberate drainage of the biliary system, for example of the gall bladder for acute cholecystitis or of the common bile duct for cholangitis, to continue for more than 10–14 days if a severe disturbance of fluid equilibrium is to be avoided.

Pancreatic Fistula is rare but may be an unexpected complication of partial gastrectomy or may follow marsupialization of a pancreatic cyst. The fluid lost varies in quantity but resembles extracellular fluid in its content of sodium and potassium and thus is liable to lead to the reduction in sodium and water content. Since pancreatic fluid contains only about half as much chloride but two or three times as much bicarbonate as extracellular fluid, a solution containing both sodium chloride and sodium lactate should be used for intravenous infusion and potassium citrate should be administered orally.

Ulcerative Colitis. In the acute phase of this disease the bouts of diarrhœa cause loss of water, sodium, and potassium in the loose mucus-laden and often purulent stools in addition to the loss of blood; there is also interference with the digestion of food and the absorption of its products. The resulting malnutrition, secondary anæmia, and chronic water and mineral depletion reduce the ability of the patient to withstand the acute phases of the disease, which the more readily result in circulatory failure because of rapid depletion of the extracellular fluid. It may be necessary to maintain circulatory volume by the intravenous infusion of dextran while blood is cross-matched. The loss of lower small intestinal and colonic secretions causes acidosis, and if intravenous infusion is necessary should be replaced by Darrow's solution; potassium citrate and sodium bicarbonate also may be given by mouth.

Large quantities of small intestinal secretions may often be rapidly lost from an ileostomy, and such fluid usually resembles extracellular fluid in its sodium content. When an ileostomy has been established for some weeks however, the sodium and chloride contents of the discharge fall. Severe diarrhœa, which may sometimes be choleraic in its intensity, may be a complication of the administration of the tetracycline drugs especially to starving patients; the control of such diarrhœa is difficult even when large doses of opium and kaolin are employed, and the intravenous replacement of the lost liquid stools

safe and satisfactory have perhaps been unusually fortunate in not having encountered patients with advanced potassium depletion.

The intravenous administration of ammonium chloride has been advised as a means of correcting the alkalosis due to prolonged vomiting since it provides chloride with a cation which is "disposable" in that the ammonium ion can be converted to urea or excreted unchanged in the urine. Such use of ammonium chloride lays the therapeutic emphasis on the wrong if the more obvious disturbance of alkalosis, rather than on the potassium deficiency which when severe, is the more important cause of illness, complications and death. When first encountered the patient may be very drowsy or even in coma; in such cases the intravenous replacement of potassium is necessary. A urinary output at the rate of at least 480 ml. per day or 20 ml. per hour should first be ensured by *the intravenous infusion of 500 ml. of 5 per cent glucose solution. Thereafter up to 2 g.* (26 mEq.) of potassium chloride (400 ml. of 0·55 per cent potassium chloride in 2·5 per cent glucose solution) may be administered over a period of 4 or 5 hours and up to 12 g. may be given during the first 24 hours. Usually only a small quantity of potassium is required to produce a marked improvement in the general condition of such patients and as soon as possible oral administration should be substituted.

After operations on the stomach or duodenum, it is occasionally necessary to continue gastric aspiration and to restrict drinking for several days because of delay in the return of normal gastrointestinal motility; this complication may persist for more than a week. Sometimes if both gastric aspiration and drinking are stopped motility returns, but rarely even this is not followed by improvement. When fear of an organic obstruction then leads to the abdomen being reopened the stoma is usually found to be wide-open and stiff with œdema and the gastric contents are swilled across it with each respiratory excursion. The cause of this complication remains uncertain but it seems to be more common in patients with prolonged severe pyloric stenosis with overt potassium deficiency. Further surgical measures except a jejunostomy are of little value, but a jejunostomy has the advantage that all aspirated fluid can be returned forthwith to the intestine, a full daily intake of calories, minerals, and protein can be resumed and intravenous infusion is no longer necessary. The stomach tube should always be removed as soon as the aspirated fluid smells wholesome and is not thickly turbid.

Duodenal Fistula. This is most common after difficult operations for duodenal ulcer when there is leakage from the closed duodenal stump or following the disruption of a gastroduodenal anastomosis; it may also occur following pancreatectomy. The fluid lost is a mixture of duodenal and pancreatic secretions and bile and is alkaline; usually sodium losses are marked and up to 2 or 3 litres of fluid may be lost in 24 hours leading to the rapid reduction of extracellular fluid and plasma volumes, hæmoconcentration, and acidosis. The volume of the daily loss usually declines with the reduction in extracellular fluid volume and increases again following the rapid administration of 0 9 per cent saline. Food and bile-stained fluid gush from the fistula a short time after eating and digestion of the surrounding skin causes severe pain. Although many duodenal fistulas close spontaneously within 7–14 days some persist and lead to repeated reductions of extracellular fluid volume. The difficulty of repeatedly replacing the lost fluid by intravenous infusions mainly arises from the differences in composition between the lost fluid and that employed for its replacement, commonly simply 0·9 per cent saline. The easiest way of avoiding this difficulty is by establishing a jejunostomy through which the collected fluid

is combined with the increased urinary output of potassium after injury, operation or infection, or if illness or loss of appetite reduces the intake of potassium, potassium depletion may occur. The association of potassium depletion with the other disabilities of such patients increases their mortality and morbidity. Although coma due to such potassium deficiency is rare it is commonly fatal; it requires urgent treatment by the intravenous infusion of a solution of potassium chloride until the patient recovers from coma. Then potassium citrate should be given orally. To prevent chronic potassium depletion potassium citrate should be given prophylactically to all patients whose ureters have been transplanted to the colon; 30 grains of potassium citrate should be taken three times a day for 3 weeks out of every four and during any illness or infection.

Acute Intestinal Obstruction. Acute primary intestinal obstruction or strangulation causes the loss of secretions into the lumen of the bowel above the level of obstruction, and the continued production of secretion is stimulated by accumulation of these secretions in the lumen of the bowel. The intestine gradually fills with fluid above the obstruction and the higher the obstruction lies in the intestines the greater is the production of secretion and the loss of fluid, principally by vomiting. In addition there is a secondary loss of inflammatory fluid into the intestinal wall and the peritoneal cavity in a quantity which varies with the nature of the obstructing or strangulating lesion. When a closed loop type of obstruction occurs, the need for surgical relief is very much more urgent than in simple occlusion, but the loss of fluid is not much greater. In strangulation there is a large loss of whole blood into the lumen, the intestinal wall and into the mesentery, and the more extensive the length of bowel affected, the larger will be the blood loss and the greater the effect on circulating blood volume.

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those patients who have their ureters transplanted to the colon, acidosis can be ited by the regular emptying of urine from the bowel every 2 or 3 hours by day and or twice during the night. The larger daily turnover of water in these patients es that they should drink up to 5 or 6 pints of water per day. Such patients do not te well the restriction of their accustomed water intake. Because acidosis is often npanied by an apparent retention of sodium with a high plasma and extracellular sodium concentration, the intake of sodium chloride should be limited to that used oking or preparing the food and none should be taken with meals; there is seldom eed to insist on a low salt diet. The excessive loss of mucus and other intestinal ions in the watery stools leads to an increased daily loss of potassium, and when this

is combined with the increased urinary output of potassium after injury, operation or infection, or if illness or loss of appetite reduces the intake of potassium, potassium depletion may occur. The association of potassium depletion with the other disabilities of such patients increases their mortality and morbidity. Although coma due to such potassium deficiency is rare it is commonly fatal; it requires urgent treatment by the intravenous infusion of a solution of potassium chloride until the patient recovers from coma. Then potassium citrate should be given orally. To prevent chronic potassium depletion potassium citrate should be given prophylactically to all patients whose ureters have been transplanted to the colon; 30 grains of potassium citrate should be taken three times a day for 3 weeks out of every four and during any illness or infection.

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Transplantation of the Ureters. The complete diversion of the daily output of urine into the pelvic colon which results from transplantation of both ureters into this segment of the bowel may be followed by disturbances of renal and intestinal function which eventually cause serious distortion of the composition of the body. The commonest form of this change is a so-called hyperchloræmic acidosis, characterized by a raised plasma chloride concentration with a lowered bicarbonate and sometimes a raised sodium concentration and rarely depression of the plasma potassium concentration. Such a disturbance occurs only in continent patients after both ureters have been transplanted. When only one ureter is transplanted and the function of the other kidney is good, urine from the bowel or an isolated pouch of bowel is always alkaline, while that from the bladder is strongly acid (Parsons *et al.*, 1952). This and other evidence suggests that perhaps the most important factor in the development of biochemical disturbances after transplantation of the ureters is one of selective reabsorption of some constituents of the urine. Such disturbances have also been attributed to impairment of renal function secondary to the dilatation of the upper urinary tract, or pyelonephritis due to infection following reflux of bowel contents and gas; such reflux is particularly common (50 per cent of cases) after direct anastomosis of the ureters by the Nesbit method but occurs in only 10 per cent of patients after indirect anastomosis of the Coffey or Stiles type (Jacobs and Stirling, 1952). Acidosis is not less common in patients with this type of anastomosis than with the Nesbit method. The common factor in all patients however seems to be the retention of urine in the colon and rectum for 4 or 5 hours by a continent anal sphincter; conversely rapid and complete recovery follows the continuous drainage of urine from the bowel by a rectal tube.

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If intravenous infusion has not been required before operation, it should seldom be necessary after operation unless there has been obvious reduction in blood volume; in such an event, the rapid infusion of 500–1,000 ml. of dextran or blood is usually sufficient to restore and maintain blood volume. If it has been necessary to restore blood volume before operation, it is a wise precaution to maintain a very slow intravenous infusion of 5 per cent glucose solution for 12 hours after operation; during this period not more than 500 ml. of solution should be administered. If however, circulatory impairment occurs, the rapid infusion of dextran or blood is then advisable without delay. Just as in burns, so in intestinal obstruction, the free administration of isotonic saline greatly increases the volume of exudate in the inflamed area of intestine. This means that œdema of the intestinal wall is greater in degree and usually lasts for a longer time than would be the case if saline were not employed. It seems possible that a good deal of ileus after acute intestinal obstruction is due to the too free use of intravenous saline. There is no reliable way of judging or calculating the quantity of sodium and water which should be administered to an individual patient, and the indications for, as well as the effects of treatment must usually be judged from the appearance and general state of the patient. The most reliable indication is the maintenance of the blood pressure and pulse rate within normal limits.

Post-operative intestinal obstruction may be due to three types of cause. Firstly, peritonitis, secondly, kinking by fibrinous adhesions, and thirdly, ileus. In peritonitis the intestines are involved in an inflammatory process and are in themselves inflamed and stiff with œdema. This inflammatory œdema limits peristalsis and leads to the accumulation of intestinal secretions in the inflamed bowel and above. The volume both of the inflammatory exudate and the accumulated secretions will be increased by the intravenous infusion of large quantities of saline. In these patients the effects of loss of intestinal secretions into the lumen of the bowel are superimposed on the reduction in total red cell mass and plasma volume which are due to the presence of peritonitis. Some benefit often follows the administration of 500–1,000 ml. of fresh blood, but the results of intravenous therapy are inconstant and unpredictable. A more conservative management of peritonitis, and of the ileus to which it gives rise, seems justified when the infection can be readily controlled by the use of the antibiotic drugs. The oral consumption of fluid should therefore be restricted. If the patient vomits, drinking should be stopped entirely and if vomiting is repeated, the stomach should be aspirated every hour. It is rarely necessary to administer fluid by intravenous infusion, and the reappearance of peristalsis and the subsidence of ileus due to inflammatory œdema is not delayed when the fluid intake is restricted as it may be when saline or glucose solution is freely administered by infusion.

The severe circulatory disturbance which is sometimes associated with advanced peritonitis following perforation of the appendix, hæmorrhagic pancreatitis or in biliary peritonitis is not much benefited by the lavish transfusion of whole blood, dextran, or isotonic saline. Some improvement has been reported in the clinical condition of these patients following the use of noradrenaline but this agent does not appear to have reduced the high mortality rate in this type of disturbance. The diagnosis of peritonitis following deliberate abdominal operations is now more difficult because the symptoms and signs are so liable to be masked by the effect of the prophylactic administration of antibiotics. The onset is now insidious and often imperceptible until a severe, but

indefinite illness develops. There is then a sudden drop in blood pressure and a rise in pulse rate with considerable reduction in circulatory volume which must be restored by the rapid transfusion of dextran or blood before exploratory operation can be undertaken. There may be much difficulty in distinguishing between ileus and organic obstruction as the cause of abdominal distension after an intraperitoneal operation. Patients with organic obstruction may for several days have been treated by gastric aspiration following a copious vomit. In such patients, before operative relief of the obstruction is undertaken, it is advisable to start an intravenous infusion in order that blood volume can be rapidly increased if circulatory failure develops during the operation. If the blood pressure has already declined before the operation is begun, it is wise to start the dextran infusion before the induction of anæsthesia. After operation a careful watch must be maintained for signs of circulatory failure. Gastric aspiration should be continued, but drinking should be forbidden. As soon as the aspirations lose their foul odour and become dark green in colour, the gastric tube should be withdrawn and should be replaced only if there is vomiting. Following an operation for the relief of this type of intestinal obstruction, it is probably an advantage to keep the patient rather short of water, and probably not more than one litre of 5 per cent glucose solution should be given in each 24 hours. Isotonic saline should be administered only if there are signs of extracellular fluid depletion. During the anxious days before peristaltic sounds are once more heard, the surgeon must exercise restraint. No good is to be achieved by allowing the patient with ileus to drink if this water is then to be aspirated from his stomach; he is better to relieve his thirst by frequently washing his mouth with ice cold water. The urinary output will be low and nothing is to be gained by increasing its volume by the intravenous infusion of large volumes of glucose solution. As soon as peristalsis is again established the patient should be encouraged to drink and eat as full a diet as soon as possible. Occasionally diarrhœa follows the relief of intestinal obstruction or ileus, and the loss of secretions may lead to rapid depletion of the extracellular fluid and to circulatory failure. If loose stools are passed tinct. opii and kaolin should at once be administered.

The use of potassium in the treatment of ileus has been repeatedly recommended. Although there is some evidence that post-operative ileus may be very common in patients who have previously been depleted of potassium, the time to treat this potassium depletion is before operation, not in the presence of an ileus. It is however safe to administer potassium cautiously from the fourth or fifth day after operation but most effect is usually obtained in patients in whom ileus has persisted for 10 days or more.

TREATMENT

General Principles. Each patient who has lost a large quantity of body fluid presents an individual problem in diagnosis and treatment. In order to regain and maintain the control of the fluid balance of such a patient, first, the present state of the patient must be assessed, secondly, the rate and direction of progression of his disturbance must be judged, and thirdly, measures to correct the disturbance must be devised.

The history and clinical appearance of the patient provide a good indication of the duration and severity of his fluid loss, in particular, evidence of reduction in the volume of blood in active circulation must be looked for since survival depends primarily on the maintenance of an adequate blood volume. Change in body weight often provides a good indirect indication of the magnitude of the total water loss. The volume and chemical

composition of the urine provides information about the compensatory changes in renal function and of the current excretory pattern. When it is altered the chemical composition of the blood also may give valuable assistance in judging the type of disturbance which has resulted, but it is important to remember that severe disturbances of whole body composition may have occurred even when the composition of the blood remains normal. The response to treatment is best judged by changes in the clinical state of the patient, in blood chemistry, blood pressure, pulse rate, and peripheral skin circulation, in the composition and volume of the urine, and whenever possible in the body weight.

The maintenance of adequate circulating blood volume by the transfusion of blood or a plasma substitute is the first measure to be considered. In many patients replacement of even large deficits of water and minerals is of secondary importance to the relief of the cause of the fluid loss; in addition, time is required for the distribution of administered solutions within the body, particularly in the case of constituents whose ultimate destination is the cells. The complete and accurate replacement by intravenous infusion of lost body fluids is impossible and the usual fluids employed omit many of the constituents which have been lost. This does not matter when small volumes of fluid are administered over short periods, but when further intravenous replacement is necessary in large volume for a long time secondary disturbances due to such inaccuracies are unavoidable. Prevention of fluid loss is therefore better than cure. Whenever possible, losses may be avoided for example by limiting the period of gastric aspiration or by returning collected fistulous discharges to the alimentary tract through a jejunostomy. It is also necessary to recognize that whatever may be administered by intravenous infusion will be dealt with in the body according to the circumstances which exist at that particular time, and that good intentions on the part of the clinician cannot alter the behaviour of the body. The only components of blood which will remain in the vessels are the red blood corpuscles. The plasma proteins and in particular, albumin, freely leave the capillaries of inflamed tissues and even those of the normal liver; crystalloid and glucose solutions equilibrate rapidly between the blood stream and the interstitial part of the extracellular fluid. Too little attention is usually paid to the composition and probable fate of the fluids which are administered to patients by intravenous infusion.

Pre-operative and Post-operative Treatment

Patients who, when admitted to hospital, are in good condition do not require special preparation for operation. Unless losses of body fluids, malnutrition or anæmia are sufficiently severe to impair the normal response to injury consequent upon operation, surgical treatment need not be delayed. When however, there is obvious malnutrition, depletion of sodium or potassium or severe anæmia, the adequate correction of these disturbances is essential well in advance of the infliction of operative injury. Not only must the lost constituent be adequately replaced, but time should be given for the body to readjust its composition to the replacement of its earlier loss, for example, the replacement of 1,000 mEq. of potassium lost by a patient with pyloric stenosis may take up to 3 weeks. Gross malnutrition implies more than mere loss of fat and protein, and in a patient with malignant disease may be difficult or impossible to correct even with the aid of fortified food mixtures. There does not seem to be any advantage in hurrying on with surgical correction of a lesion if healing is almost certain to be impaired by previous protein, vitamin or mineral depletion Because of the risk of

hæmolysis and pyrexial reactions, correction of anæmia by the transfusion of whole blood or packed cells should always precede the operation by a number of days.

In the average patient, a normal intake of food and fluid is usually maintained until about 24 hours before operation and then the diet is reduced. Small quantities of fluid should be provided even early on the day of operation. In temperate climates there is now less tendency to employ intravenous infusions as a routine procedure after all major operations. While such administration of fluid may be necessary in continental countries with extremes of temperature and humidity, the very equable environment of a temperate climate seldom calls for a large volume of daily fluid intake, and most patients seem well able to tolerate marked restriction or even the stoppage of their water intake for up to 48 hours after major operations When gastric aspiration is employed after operations on the alimentary tract, the oral consumption of fluid should be stopped, but this restriction should be maintained only so long as it is necessary to keep the stomach empty, individuals vary widely in this respect, but it is usually possible, even after partial gastrectomy, to resume the oral consumption of water within 48 hours of operation.

In order that deviations from the normal post-operative progress may be more readily recognized, it is advisable to keep an accurate record of all urine passed as well as all fluid consumed or infused. The value of such urine records is greatly increased if specific gravity is measured as well as the volume. In this way abnormality of renal function and impending failure can be more readily recognized. After operation, the continuous intravenous infusion of fluid should be employed only when there is good reason for its use. Unless there is a large fluid loss in addition to the urine and insensible water loss, the initially well nourished and undepleted patient seldom requires to be given fluid by infusion.

When extra-renal loss by gastric aspiration, by drainage from a fistula, or by diarrhœa is excessive, and the consumption of fluid and food by mouth must be restricted, there is good justification for the employment of intravenous replacement. The volume and composition of the fluid must be as closely related to those of the losses as possible. Average figures for the composition of gastric and intestinal secretions are shown in Table 4, and these quantities are a satisfactory basis for constructing a suitable replacement mixture if it is impossible to analyse the composition of the fluid actually lost by a particular patient. The volume of the fluid lost must however be as completely collected and accurately measured as possible. The detailed management of disturbances of sodium, potassium, and water content of the body have been dealt with in the earlier sections.

Maintenance of Nutrition

The healthy adult at rest in bed probably requires at least 2,000 calories per day, and for several days after injury this basal requirement may be much increased. The ideal mixed diet should contain sufficient protein to provide 12·5 per cent of the total calories (70 g. in a 2,240 calorie diet). The proper utilization of protein depends on the simultaneous provision of sufficient non-protein calories to prevent the use of protein for energy purposes and thus its wastage as a source of protein components. This dietary principle applies no matter how the protein or its components and their accompanying calories are administered.

Parenteral Feeding. This term implies the complete provision by intravenous infusion of the daily requirements of calories, protein, minerals, and vitamins. The chief limiting

composition of the urine provides information about the compensatory changes in renal function and of the current excretory pattern. When it is altered the chemical composition of the blood also may give valuable assistance in judging the type of disturbance which has resulted, but it is important to remember that severe disturbances of whole body composition may have occurred even when the composition of the blood remains normal. The response to treatment is best judged by changes in the clinical state of the patient, in blood chemistry, blood pressure, pulse rate, and peripheral skin circulation, in the composition and volume of the urine, and whenever possible in the body weight.

The maintenance of adequate circulating blood volume by the transfusion of blood or a plasma substitute is the first measure to be considered. In many patients replacement of even large deficits of water and minerals is of secondary importance to the relief of the cause of the fluid loss; in addition, time is required for the distribution of administered solutions within the body, particularly in the case of constituents whose ultimate destination is the cells. The complete and accurate replacement by intravenous infusion of lost body fluids is impossible and the usual fluids employed omit many of the constituents which have been lost. This does not matter when small volumes of fluid are administered over short periods, but when further intravenous replacement is necessary in large volume for a long time secondary disturbances due to such inaccuracies are unavoidable. Prevention of fluid loss is therefore better than cure. Whenever possible, losses may be avoided for example by limiting the period of gastric aspiration or by returning collected fistulous discharges to the alimentary tract through a jejunostomy. It is also necessary to recognize that whatever may be administered by intravenous infusion will be dealt with in the body according to the circumstances which exist at that particular time, and that good intentions on the part of the clinician cannot alter the behaviour of the body. The only components of blood which will remain in the vessels are the red blood corpuscles. The plasma proteins and in particular, albumin, freely leave the capillaries of inflamed tissues and even those of the normal liver; crystalloid and glucose solutions equilibrate rapidly between the blood stream and the interstitial part of the extracellular fluid. Too little attention is usually paid to the composition and probable fate of the fluids which are administered to patients by intravenous infusion.

Pre-operative and Post-operative Treatment

Patients who, when admitted to hospital, are in good condition do not require special preparation for operation. Unless losses of body fluids, malnutrition or anæmia are sufficiently severe to impair the normal response to injury consequent upon operation, surgical treatment need not be delayed. When however, there is obvious malnutrition, depletion of sodium or potassium or severe anæmia, the adequate correction of these disturbances is essential well in advance of the infliction of operative injury. Not only must the lost constituent be adequately replaced, but time should be given for the body to readjust its composition to the replacement of its earlier loss, for example, the replacement of 1,000 mEq. of potassium lost by a patient with pyloric stenosis may take up to 3 weeks. Gross malnutrition implies more than mere loss of fat and protein, and in a patient with malignant disease may be difficult or impossible to correct even with the aid of fortified food mixtures. There does not seem to be any advantage in hurrying on with surgical correction of a lesion if healing is almost certain to be impaired by previous protein, vitamin or mineral depletion. Because of the risk of

cent fat emulsion over about 3 hours. An infusion of 500 ml. of a 5 per cent amino acid and 5 per cent glucose solution should last about 4 or 5 hours If alcohol also is being used, 500 ml. of a 6 per cent solution containing 30 ml. of ethyl alcohol can be completely oxidized by an adult in 3 hours.

The usual solutions of amino acids and carbohydrate contain little sodium or potassium and negligible amounts of anions. Because of the absence of other constituents necessary for the formation of protoplasm, such as potassium and phosphate, it has been suggested that these solutions are probably of limited value Nevertheless, it has been shown (Abbott *et al.*, 1955) that when amino acids, accompanied by adequate calories as fat, were administered by intravenous infusion to previously well nourished patients after partial gastrectomy, the catabolism of body protein could be considerably reduced. There is however at present no justification for the routine administration of such solutions after operation. The administration of a 5 per cent glucose solution does not alone prevent protein catabolism after surgical injury, although it may help to make fat oxidation more complete and to some degree reduces the effect of starvation on protein catabolism.

The indications for intravenous feeding with fat emulsions and amino acids are limited to the few states in which a patient is for a long time unable to eat or digest food, for example in the treatment of ulcerative colitis or fistulas of the small intestine.

Jejunostomy. Jejunostomy feeding has many advantages in surgical patients. In œsophageal obstruction it allows of the maintenance of a high intake of protein and calories before and throughout the post-operative period until eating can be resumed. Provided it is made in a rather lower loop than usual, its use does not interfere with the free choice of a loop of jejunum for œsophageal anastomosis. Subjective symptoms are fewer with a jejunostomy than with a gastrostomy, and regurgitation does not occur. It is of particular value in patients with gastric, duodenal, biliary, or pancreatic fistulas, for not only can the discharge from the fistula be collected and replaced in the intestine through the jejunostomy, but an ample intake of water, food, minerals, and vitamins can be maintained through the jejunostomy, and the need for intravenous infusion obviated. A Witzel type of jejunostomy may be made under local anæsthesia and the first feed of 120 ml. of 5 per cent glucose solution should be injected before the wound is closed. Thereafter, 2 hourly feeds are given containing at first 60 ml. of milk mixture followed by 60 ml. of 5 per cent glucose solution or water. After 12 or 24 hours the quantities can usually be increased to 90 ml. each of milk mixture and water, and then to 120 ml. of each. In this way a total water intake of 2,800 ml. per 24 hours can be achieved.

Cramping pain is usually due to the use of hypertonic feeds. Diarrhœa is often troublesome, no matter what kind of feed is used and is best controlled by the administration of tinct. opii (15 minims 4 to 6 times a day according to need) and kaolin (1 oz. every 4 hours washed into the tube with water). The best feed is a simple mixture of 2 pints of fresh milk, 240 g. lactose, and 200 g. dried skimmed milk powder which provides 2,400 calories, 120 g. protein, 76 mEq. of sodium, 116 mEq. of potassium and 90 mEq. of chloride. The addition of a vitamin supplement makes this mixture adequate for nutrition for several weeks. When there is potassium deficiency, up to 12 g. potassium chloride (156 mEq. potassium) may be added per day to the water used to wash the tube after feeds. Sodium chloride should not be added to the feeds as it usually causes diarrhœa. Fistulous discharges should be run into the jejunostomy between feeds, the tube being washed clean with water before a feed is given.

factors in the supply of sufficient calories are the total volume of fluid which can be tolerated by intravenous infusion and the concentration of the energy source in that fluid. For example, when glucose solution is employed, there is in the normal adult a rapid diuretic response to the infusion of a 5 per cent glucose solution; this diuretic response is reduced after injury and if more than 2·5 litres of glucose solution are administered per day some of the water is retained. When stronger solutions of glucose are employed, up to 30 per cent of the glucose may be lost in the urine. Such glycosuria is less with fructose than with glucose because fructose is more rapidly extracted from the blood. Slow infusion of concentrated glucose solution (40 per cent) into the great veins allows the provision of 1,500 calories per day in a total volume of only 1 litre, but this type of infusion is not free of risk and is unsuitable for routine post-operative use; it should be employed only in anuric patients.

A 15 per cent fat emulsion will provide 1,200 calories per litre; safe and satisfactory commercial fat emulsions for intravenous infusion should soon be available. Ethyl alcohol has also been employed as a source of calories, being infused in a 6 per cent

TABLE 5. QUANTITIES OF FAT CARBOHYDRATE AND ALCOHOL NECESSARY TO SUPPLY 2,100 CALORIES PER 24 HOURS

	Calories/g.	Solution per cent	Litres per 24 hours
262 5 g. fat	8 0	15	1·75
560 g. glucose or fructose	3·75	5 10 40	11·2 5 6 1·4
300 g. ethyl alcohol (375 ml.)	7 0	6	6 25

solution, 3 litres of such a solution have been repeatedly administered in 24 hour periods without adverse effects (Wilkinson, 1955). The quantities of fat, carbohydrate and alcohol necessary to supply 2,100 calories per 24 hours are shown together with the volumes of fluid in which they must be dissolved in Table 5. For intravenous infusion, whole protein must be prepared by hydrolysis to amino acids and small peptides; milk or meat protein is hydrolysed by acids or enzymes, and any deficiency of essential amino acids are made up by the addition of supplements. In the past solutions containing 5 or 10 per cent amino acids combined with glucose have usually been used, but unless a fat emulsion or some other additional source of energy is also administered, it is difficult to ensure that the amino acids are not deaminated and used for energy purposes. In addition, rapid infusion of amino acid solutions leads to much wastage of both the nitrogenous material and the glucose in the urine, but a slower infusion of solutions containing glucose causes greater discomfort to the patient and is frequently followed by chemical thrombophlebitis. The basal daily requirement per 1·73 square metres of body surface is about 10 g. of nitrogen and 1,600 calories; in clinical use an attempt is usually made to administer 70–80 g. of protein (11·2–12·8 g. of nitrogen) and 1,800–1,900 calories. It is unsafe to administer fat emulsions through the same tubing and at the same time as amino acid and glucose solutions, and it is probably best to give the fat first, administering 500 ml. of a 15 per

cent fat emulsion over about 3 hours. An infusion of 500 ml. of a 5 per cent amino acid and 5 per cent glucose solution should last about 4 or 5 hours. If alcohol also is being used, 500 ml. of a 6 per cent solution containing 30 ml. of ethyl alcohol can be completely oxidized by an adult in 3 hours.

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Replacement and Maintenance of Water and Electrolyte Content

Water. The immediate daily water requirement of 1,500 ml. can readily be supplied by the intravenous infusion of 5 per cent glucose solution. There does not seem to be any good reason for administering more than the minimum of requirements under average conditions. When however abnormal losses of water are due to unusual environmental conditions, some extra water should be provided. It is probably better to give too little than too much, especially after operation. Glucose solution should not be used as a replacement for sweat loss or in the loss of fluids containing minerals. It is too commonly thought that glucose solution is relatively innocuous and readily excreted. In anuric patients except when necessary during the diuretic phase, the administration of glucose solution is dangerous, and it is also liable to produce water intoxication when administered rapidly during the oliguria which normally occurs after operations and in the presence of severe infection of any kind, especially if renal function is chronically impaired. Minimum daily water requirements persist even when large volumes of other kinds of fluids are being administered to the patient, and if an attempt is being made to supply the fluid requirements of the body completely by intravenous infusion due allowance for the purely water requirements must be made. This applies even when restrictions of intake have been imposed because of œdema.

Sodium. Sodium is most commonly employed as a solution of sodium chloride in varying strengths. Isotonic saline (0 9 per cent) contains 153 mEq. per litre of sodium and of chloride and is therefore hypertonic compared with the average sodium (140 mEq. per litre) or chloride (103 mEq. per litre) concentrations in extracellular fluid. This solution however, is almost isotonic with the total cation and anion in extracellular fluid (155 mEq. per litre). Because of this high sodium content, isotonic saline is most often used to replace an acute loss of extracellular fluid. In this case it provides an excess of chloride and tends to produce acidosis which is usually compensated by an increased renal excretion of chloride. The rapid infusion of isotonic saline increases the plasma volume for a short time, but at least three-quarters of the administered fluid is rapidly lost from the vessels into the interstitial fluid. There are various weaker solutions of sodium chloride which have been devised to be used when the water requirement exceeds that of sodium. By using such solutions it is possible to prescribe only one mixture throughout the 24 hours and to maintain a continuous infusion of steady composition. These weaker solutions of saline usually contain glucose and now are commonly prepared by mixing varying volumes of 0·9 per cent saline and 5 per cent glucose solution. "Half normal" saline (0·45 per cent) contains equal volumes of 0 9 per cent saline and 5 per cent glucose solution. "Fifth normal" saline contains 0 18 per cent sodium chloride and is made by mixing 4 pints glucose solution with 1 pint of 0·9 per cent saline; it is widely used in pædiatric practice as a means of compensating for the poorer renal capacity of infants to conserve sodium. Hypertonic saline is mainly used in the treatment of water intoxication, but has more recently been employed for the restoration of large sodium deficits; a 5·85 per cent solution has the advantage that it contains 1 mEq. of sodium and of chloride per millilitre of solution.

Glucose Saline. The combination of 5 per cent glucose and 0 9 per cent saline results in a hypertonic solution. Its alleged advantage is that it provides calories by the administration of glucose, but this is possibly outweighed by the intracellular dehydration which it causes.

Sodium Lactate. An isotonic solution (1/6 molar or 1·86 per cent) contains 166 mEq. of sodium and of lactate per litre. It is used in sodium deficiency to provide sodium in combination with an anion which can be readily catabolized, it is thus of value in increasing the proportion of cation to anion and hence the reduction of acidosis. It is most commonly used combined with sodium and potassium chlorides in such compound solutions as Darrow's solution and Ringer lactate.

Potassium. An isotonic solution of potassium chloride contains 1·1 per cent potassium chloride (149 mEq. potassium per litre). This is too high a concentration of potassium for safe use, and it is usual to mix equal parts of such a solution with 5 per cent glucose solution to give a concentration of 0 55 per cent potassium chloride or 74 mEq. of potassium per litre. The rate at which potassium can safely be administered depends on the metabolic state of the body and to some extent on the degree of deficiency which exists. In coma, 2 g. potassium chloride (26 mEq. potassium) may be given by intravenous infusion over a period of 4 hours and this should be enough to arouse the patient from coma and to increase the output of urine. Because of the danger of potassium intoxication, most fluids contain only small concentrations of potassium.

Compound Electrolyte Solutions. In an attempt to replace more accurately the complicated loss of electrolytes which are common in clinical practice, various combinations have been made. Most of these solutions were originally devised for use in limited circumstances and their subsequent wider employment often for purposes for which they are not really suitable, is one reason for the poor results which often follow their use.

Hartmann's Solution. (Saline lactate.) This solution contains sodium lactate in addition to sodium chloride (0·6 per cent) to reduce the excessive content of chloride in proportion to sodium in isotonic saline (157 mEq. sodium, 102 mEq. chloride and 55 mEq. lactate per litre) It may be used with advantage in the treatment of sodium and chloride losses by vomiting.

Ringer Lactate. In this solution potassium chloride and calcium chloride have been added to the sodium chloride and sodium lactate of Hartmann's solution (129 mEq. sodium, 4 mEq. potassium, 4 mEq. calcium, 110 mEq. chloride, 27 mEq. lactate per litre) and it is now used in the treatment of acidosis and potassium deficiency. Its content of potassium is too low to be of value in the treatment of a large deficit.

Darrow's Solution was originally introduced for the treatment of infantile diarrhœa. This solution contains a mixture of sodium chloride, potassium chloride, and sodium lactate (123 mEq of sodium, 35 mEq. of potassium, 103 mEq. of chloride, 55 mEq. of lactate per litre). Govan and Darrow (1946) recommended that for intravenous administration to babies this solution should be diluted with 5 or 10 per cent glucose solution, but this is unnecessary in adults. This solution can be used for the treatment of potassium deficiency and at the same time will increase extracellular fluid volume and diminish acidosis. Various other compound solutions some of which may contain magnesium and phosphate as well as sodium chloride and bicarbonate and potassium chloride have been devised, and experience of their use is accumulating, but at present it is difficult to judge their value.

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CHAPTER XIV

HÆMORRHAGE, SHOCK AND THE ILLNESS OF TRAUMA

RUSCOE CLARKE

INTRODUCTION

THE first consideration in the care of the majority of injured patients must be the prevention and treatment of hæmorrhage and the early clinical disturbances known as "shock."

There is little doubt that even in minor injuries the systemic response involves both nervous and endocrine systems, but the present state of our knowledge warrants consideration of this response primarily in terms of the circulation.

Even from this limited point of view it is already clear that many of the physiological, pathological, and clinical changes which may develop later are related to the events of the acute phase.

Grant and Reeve (1951) in their research report of observations made during the Second World War attempt to discard the word "shock." They discuss the early circulatory patterns of the "illness of trauma." It is certainly important that the word "shock" should never be used as a clinical description without amplification in terms of detail of symptoms and signs. The significance of such signs is being clarified by the study of their association with measureable changes in the quantity, composition, and distribution of circulating blood. The nature of the illness of trauma is becoming clearer as its features are studied in association with the circulatory phenomena of the acute phase of injury.

An interesting account of severe traumatic shock was given by Ambroise Paré (1510–90) who attributes the condition to *bleeding*, "*fear or tumult*" or "*corruption*" from "*poisonous wounds*." This general classification is still relevant although increasingly during the last 40 years it has been possible to unravel the contribution which a variety of factors can make to a particular clinical state of collapse following injury. We no longer attempt to consider "shock" as a single entity with a single cause, although it is still true that the whole clinical state may be due to loss of blood or other fluid from the circulation, to the effect of nervous stimuli, or to severe infection. In the early stages of injury there is no doubt that the most important factor contributing to any serious state of shock is *oligæmia*, a low blood volume, resulting from loss of blood or other fluid from the circulation.

CLINICAL FEATURES

Hæmorrhage

A mass of experimental work on animals, many studies on blood donors and human volunteers, and clinical observations with blood volume studies on patients who have received accidental or surgical trauma, provide us with a picture of the effects of bleeding.

Sudden severe bleeding of 40-50 per cent of total blood volume is likely to be immediately fatal. Loss of the same volume of blood more slowly allows compensatory mechanisms to maintain the circulation although the organism may later develop fatal sequelæ. Severe hæmorrhage leads to a clinical state in which the patient is pale or grey, cold, with a thin thready rapid pulse and a very low blood pressure (systolic below 50-60 mm. Hg.). Consciousness may be lost or the patient may be in a state of obvious anxiety, breathing may be shallow or rapid and air hunger present, sweating may be copious and vomiting is not infrequent. Without transfusion rapid deterioration and death are likely.

Lesser degrees of sudden bleeding and moderately severe bleeding which occurs more slowly, give rise to a less severe clinical state of collapse. Pallor is common and the extremities are likely to be cool. The pulse rate may be raised to over 100 per minute; the systolic blood pressure may fall to between 70 and 100 mm. of mercury. Anxiety is not always present and there may be few other symptoms. Consciousness is not necessarily disturbed. If bleeding ceases recovery is likely in the absence of other harmful factors. Lesser degrees of bleeding up to 25 per cent of total blood volume can be associated with no obvious systemic signs but such patients are liable to collapse following further bleeding, movement, anæsthesia, or other interference.

Observations on blood donors and volunteers have shown that a proportion of patients will collapse following withdrawal of a pint of blood or less. This collapse is frequently of the "vasovagal" type with a slow pulse. The phenomena appears to be closely related to the ordinary faint and recovers spontaneously if the patient is kept flat. The response is operated through a nervous reflex and involves a redistribution of blood with probable widespread increase in blood flow through muscles. The blood pressure falls, and it is possible that this reaction should be regarded as a response to bleeding which can be beneficial in so much as the fall in blood pressure allows clotting in a bleeding vessel to take place more rapidly. The response, however, may be evoked not only by bleeding but by a whole range of associated stimuli including the sight of blood, the prick of a needle, or even the thought of the prick of a needle! With larger measured bleedings the proportion of patients who collapse increases with the amount of blood withdrawn.

Hæmorrhage and Trauma

Whilst in fact no hæmorrhage is likely to take place in the total absence of trauma, it has long been felt by many observers that the clinical pattern exhibited by patients with serious injuries differs in some ways from that due to pure hæmorrhage. This is certainly only a question of degree. The development of modern blood volume techniques has shown that a large variety of injuries, including battle casualties with deep wounds and civilian injuries with closed fractures, lose blood to a much greater extent than had previously been recognized. Grant and Reeve suggested that the extent of tissue damage constituted the best initial guide to the extent of blood loss and the degree of oligæmia present. They attempted to define their observations in terms of volumes of damaged tissue using the hand or fist as a crude measurement. They classified wounds into "small" with a volume of tissue damage "less than one hand"; "moderate" with tissue damage "one to three hands"; "large" with tissue damage to "3-5 hands"; and "very large" with tissue damage "more than 5 hands."

This approach is useful but in closed fractures where the extent of tissue damage is less obvious than in many battle casualties, it is probably best to think in terms of the

actual volume of primary swelling (Clarke, Topley, and Flear, 1955). The extent of primary swelling has been found to be closely related to the loss of blood from the circulation. A fracture of the os calcis or ankle with immediate swelling may lose as much as a pint of blood (½ litre) into the tissues. Moderately severe fractures of the tibia and fibula can lose 1–3 pints (½–1½ litres); fractures of the shaft of the femur can lose 1–4 pints (½–2 litres) and frequently *much* more. Fractures of the upper limb usually lose less but considerable swelling may indicate significant hæmorrhage. Bleeding in association with trunk injuries, particularly fractures of the pelvis, is more difficult to assess but may be very great indeed.

Patients with open fractures vary considerably in the amount of blood lost at the time of injury and subsequently into dressings but on average lose at least twice as much blood as similar fractures without an associated skin wound.

Clinical estimates of blood loss carried out in association with blood volume studies have indicated that hæmorrhage is an all important factor contributing to states of "shock" in the overwhelming majority of wounds, fractures and soft tissue injuries. In the absence of open wounds this closed hæmorrhage may take place more slowly than when moderate or major blood vessels are openly divided, but hæmorrhage can be massive and its effects must be appreciated. The clinical pattern of response is to a considerable extent similar to that which follows straightforward hæmorrhage, but other features of the injury including pain, tissue damage and involvement of important viscera, complicate and modify the picture.

Even in the absence of obvious bleeding the injured patient first seen with a pulse rate of 140 or over, systolic blood pressure 60 or less, pale or grey, and cold and sweating, must be regarded as suffering from major hæmorrhage. Such a patient requires transfusion just as urgently as where hæmorrhage is obvious. This clinical picture is rarely produced without a blood loss of the order of 40–50 per cent, and the transfusion ultimately required is frequently of the order of total blood volume (4–7 litres, 7–13 pints) or more.

A lesser degree of blood loss associated with wounds and fractures may be equally important, particularly where surgery is required for the treatment of the injuries. In the past such patients have frequently collapsed as a result of interference and the collapse has been attributed to neurogenic effects. It is now clear that the oligæmic patient is much more likely to respond adversely to a variety of stimuli, than is the patient with a near normal blood volume.

PHYSIOLOGICAL AND PATHOLOGICAL CHANGES

Compensation and Circulatory Failure

One of the difficulties that has complicated an understanding of the acute circulatory response to trauma has been a tendency to confuse physiological responses of an adaptive or homeostatic nature which can benefit the organism and tend to assist survival, with superficially similar reactions which are not beneficial and can lead to progressive irreversible pathological changes.

Much animal experimental work has been concerned with the study of "irreversibility" in states of shock produced by a wide variety of agents including blood loss. Recent clinical and experimental research has been more concerned with the earlier changes at a stage when they are likely to be reversible.

Gradual blood loss to less than 20 per cent of the total blood volume in man does not necessarily produce any fall in blood pressure. Not infrequently it causes mild hypertension. Sometimes only the diastolic pressure is raised. In the absence of bradycardia associated with fainting, blood loss of this order is likely to result in a small but perceptible increase in pulse rate.

The effect of a 20 per cent blood loss on cardiac output is variable with a tendency for it to fall. It is assumed that an initial loss of blood leads to a transient drop in arterial blood pressure which in turn evokes an increase in peripheral resistance through a reflex arc originating in the carotid sinus and aortic areas. Blood loss of this order produces a fall in pressure in the right atrium, central veins and pulmonary artery. The left atrial pressure falls at first but tends to level off. Recent evidence suggests that the heart and lungs constitute in man a reservoir of blood which is decreased in orthostasis, moderate bleeding and under anæsthesia. Half a litre of blood or more can be transferred from the pulmonary circulation without evidence of any disturbance of function.

The spleen in dogs probably acts as a useful reservoir of blood which empties in response to bleeding. This certainly does not occur to the same extent in man, although moderate hæmorrhage probably results in some decrease in blood content of liver, spleen and portal venous system.

In general it appears that blood loss of 10–20 per cent can be compensated by circulatory redistribution without producing any obvious clinical disturbance. So long as the total decrease in blood volume does not exceed 20–25 per cent such states are often spontaneously and rapidly reversible without transfusion. Further blood loss up to, for example, 30–40 per cent of total blood volume leads to a further reduction in venous return, decreased cardiac output, an increased pulse rate, and a falling blood pressure. The blood pressure may, however, be maintained at a normal level or even above, with increased peripheral resistance and reduction in blood flow to vital organs. This can result in ischæmic anoxia of the kidney, liver, heart, lungs, brain and endocrine organs, and any of these may be concerned at some stage of the downward path, with the determination of irreversibility and death.

In any case continued bleeding leads to anoxia and a diffuse interference with cellular function, stasis, increased capillary permeability, further anoxia and finally a total failure of capillary tone—true peripheral circulatory failure. In the final state no amount of transfusion can restore the blood pressure and the patient continues to bleed to death into his own capillary bed. At the same time anoxia may affect the heart muscle and cardiac failure contribute to the process of deterioration.

In moderate bleeding there is an important additional compensatory mechanism—the absorption of fluid, electrolytes and subsequently of protein into the circulation from the tissues. This leads to an increase in plasma fluid and total blood volume, to hæmodilution, a falling hæmatocrit and anæmia.

This increase in blood volume frequently allows the peripheral circulation to be maintained but with blood which has lost a proportion of its red cells and oxygen carrying capacity. In severe or progressive hæmorrhage this can only be partially effective in maintaining the health of the organism. Survival is dependent not only on blood volume *per se* but on the maintenance of a proportion of red cells to plasma, whose lower limit will depend on a number of particular circumstances in any given individual. It follows that where blood has been lost, plasma is only of partial value in resuscitation.

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Gas Gangrene. In the presence of damaged or devascularized muscle, particularly in battle casualties, gas gangrene can develop with great rapidity and lead to a state of severe peripheral circulatory failure almost indistinguishable from advanced hæmorrhagic shock, within 4–6 hours of injury. Blood loss contributes to this condition and fluid is extravasated into the tissues in the vicinity of the infection. The total effect is partly due to toxic products derived from the site of infection, which reinforce the effects of fluid loss. In most cases the condition can only be reversed by radical removal of infected muscles or by amputation.

Fulminating Infections. Severe or rapidly developing states of septicæmia can lead to a clinical picture of "shock." Following injury this is predisposed to by blood and fluid loss but involves in addition a widespread loss of vascular tone with stasis and finally capillary paralysis.

When the cause of the condition can be removed or treated by chemotherapy, the clinical state may be improved by the use of such drugs as Noradrenaline in combination with fluid replacement.

Respiratory Obstruction and Lung Complications. Sudden obstruction to respiratory passages associated with severe anoxia can lead to a state of shock which is largely reflex in origin. Partial obstruction to respiratory passages from trauma or œdema and more frequently from aspiration of blood or vomit will contribute to anoxia and increase the effects of associated oligæmia. Damage to the thoracic cage interfering with normal respiratory function, with or without lung damage, hæmothorax, or pneumothorax, can reflexly produce a state of coldness and pallor. There is a tendency for the blood pressure to be normal or high with vasoconstriction of arteries and veins. In such circumstances oligæmia may be difficult to treat, transfusion may produce venous distension of neck veins in the presence of a low blood volume. Aspiration of blood or vomit will in addition predispose to changes in the lungs themselves. Such changes in addition to those resulting from direct injury or bronchial irritation predispose to pulmonary œdema. The danger is likely to be increased in the presence of oligæmia from whatever cause.

A number of patients with major abdomino-thoracic injuries appear to improve following transfusion but subsequently deteriorate in a way which suggests that direct interference with the functions of the heart and lungs are largely responsible for the clinical state and the failure to respond to restoration of blood volume.

Head Injuries. Head injuries complicate the clinical response to injury. They are frequently associated with bleeding from the nose, mouth, or base of skull, and in the presence of any degree of unconsciousness or diminution of the cough reflex blood is likely to trickle down into the trachea. The resulting anoxia may increase the depth of unconsciousness. Sometimes the process can be reversed by endo-tracheal aspiration when it becomes clear that the cerebral damage itself was minimal. Patients with open head injuries can bleed profusely from scalp lacerations or from fractures of the base via the nose and mouth. Such bleeding is difficult to estimate when the blood is swallowed. In the presence of even slight head injuries it is easy to overlook associated injuries which may be associated with bleeding into the tissues. In more severe head injuries, major abdominal hæmorrhage, for example, may be present in the absence of any signs or symptoms. Head injuries by themselves never present the typical picture of oligæmic shock, and whenever this is present it must be presumed that hæmorrhage has taken place. The existence of brain damage is never any contra-indication to the treatment of

Complications of Blood Loss

In moderate hæmorrhage when bleeding has been stopped and other features of the injury do not lead to progressive systemic upset, recovery is frequently straightforward. The blood volume is partially restored over a period of hours and days, the plasma proteins are subsequently increased and finally the red cell volume is restored by production of new red cells. The period of recovery may be complicated by symptoms of anæmia, e.g. dyspnœa on standing or exertion. Hæmorrhage alone produces a metabolic disturbance although this may be of relatively short duration. A period of hæmorrhagic oligæmia of 1–2 hours or more, may produce a transient or even serious disturbance of renal or hepatic function. The former is particularly likely to be dangerous if there exists any other source of renal damage. In old people, and in fact in all patients with underlying pathology of the cardiovascular system, even a short period of severe oligæmia may predispose to the development of phlebothrombosis, coronary or cerebral thrombosis, renal failure, pulmonary œdema and bronchopneumonia.

When hæmorrhage is associated with major trauma, a number of factors may be introduced which combine with the effects of hæmorrhage to produce a variety of pathological complications. In the presence of severe tissue damage and particularly where the vessels supplying limbs, muscles or other organs are damaged, oligæmia and anæmia contribute to the effect of the trauma on the tissues and increase the danger of tissue necrosis. An inadequate supply of blood in any injured part will predispose to the development of infection, and where muscles are damaged to the onset of anærobic myositis. Blood loss and anæmia can lead to delay in wound healing. Severe tissue injury can result not only in local bleeding but in local extravasation of fluid which tends to increase the risk of oligæmia; although in more moderate closed injuries it is probable that fluid and electrolytes are reabsorbed from the site of bleeding even whilst further loss of whole blood is still taking place. When the injury directly involves vital organs the effect of such damage will be increased by circulatory inadequacy resulting from untreated hæmorrhage.

In addition to the specific effects of particular injuries, the combination of blood loss and trauma gives rise to general metabolic and other disturbances which are at least in part preventable or reversible by appropriate treatment of oligæmia.

Contributory Factors

General. Whatever the nature of the injury and the extent of blood loss, the systemic response may be adversely influenced by exposure, fatigue, dehydration, and pre-existent malnutrition or disease.

Intestinal Injuries. Penetrating wounds or closed rupture of the intestinal tract may produce a state of apparent shock reflexly from irritation to the peritoneum although this is likely to be transitory in the absence of fluid loss. Intestinal lesions are in addition associated with fluid loss into the lumen and tissues of the gut, and as peritonitis develops fluid is poured out into the peritoneal cavity. In some cases an enormous loss of fluid can occur rapidly and it may be difficult to distinguish such loss from peritoneal hæmorrhage except at laparotomy. At a later stage following abdominal injury, the development of paralytic ileus can be associated with gross extravasation of fluid into the lumen and tissues of the gut, with oligæmia and in the absence of significant hæmorrhage, a raised hæmatocrit.

injury should ever be given anything by mouth. The traditional hot sweet tea should be confined to those patients who have been shaken up but have obviously not sustained any important injury.

There is no place for any artificial heating in the first-aid treatment of the injured. An ordinary warm blanket may make a patient more comfortable but hot water bottles or hot cradles are never indicated. All movements should be carried out as gently and steadily as possible. The patient should be left alone as much as possible until he can be transferred to a stretcher. If there are signs of severe hæmorrhagic shock the legs should be raised so that the blood can drain down towards the head. Obvious fractures should be splinted, wounds should be covered and bandaged without any attempt at other local treatment. Severe bleeding can nearly always be stopped by firm bandaging over gauze or wool. Tourniquets are very, very seldom of any use. If severe hæmorrhage cannot be stopped without the application of a tourniquet and the patient is not in a desperate condition, the tourniquet can advisably be released a few minutes after firm bandaging of the wound. Urgent action at the first-aid level is required only for:

(1) Sucking wounds of the chest.
(2) Respiratory obstruction or cessation of breathing.
(3) Severe external hæmorrhage.

Diagnosis

On arrival at hospital the first step in *treatment* is the establishment of a provisional *diagnosis*. This involves assessment of the patient's general condition, of the probable extent of blood loss and site of injuries.

When it is clear that severe injuries are present or that the patient is in a severe state of collapse, a provisional assessment only can be made in the first place. Once it is clear that blood loss is a major contributory factor to the patient's condition, the next step will involve preparation for transfusion.

In moderate injuries a short period should be allowed to observe changes, which frequently may be in the direction of improvement. Most patients with a systolic blood pressure greater than 70 mm. of mercury can with advantage be kept under observation for at least a quarter to half an hour before transfusion is decided upon. Only in states of severe shock, obvious progressive bleeding or in the presence of deterioration, should transfusion be started immediately. When it is suspected that early transfusion is likely to be needed, blood should be taken for crossmatching and an intravenous drip set up with saline, so that transfusion can be started as soon as blood is available or the clinical condition clearly indicates the need.

Following a short period of observation a plan for treatment must be made which involves the timing of detailed investigations including X-rays, in relationship to transfusion and possible indications for early surgery.

There are times when the nature of the injury makes it clear that only a limited examination is necessary to define its extent, but there are many types of injury which require detailed examination of the whole body. This is particularly necessary in battle casualties, road accidents and falls from a height. Major injuries to deep structures may present no signs or symptoms of any kind, when they are associated with painful lesions elsewhere. Relatively major lesions can be overlooked because other injuries appear at first to be more serious and require urgent attention. Minor degrees of cerebral damage with

associated hæmorrhage and the cerebral state is likely to be improved by restoration of the circulation to normal. On the other hand severe anoxia from abdominal or other internal bleeding can lead to extreme violence and a diagnosis of cerebral irritation with delay in starting urgently needed transfusion.

Spinal Injuries. Major injuries to the spinal cord with paraplegia, can lead to pallor with a low blood pressure and a feeble pulse, as a result of paralysis of the nerve supply to the vascular tree, similar to the collapse which may follow high spinal anæsthetics. This is more likely to occur in the presence of a fracture of the spine which itself may give rise to considerable bleeding.

Painful Stimuli. A variety of clinical states can result from painful stimuli, particularly from prolonged direct nerve irritation. Experimentally a prolonged fall of blood pressure can be produced in animals by stimulation of peripheral afferent nerves. Such states become much more dangerous in the presence of moderate oligæmia produced by bleeding. In man a sudden collapse in the presence of oligæmia may be attributable to painful movement, but it is more common for painful stimuli to be associated with an elevated blood pressure in the presence of moderate hæmorrhage. This elevation of blood pressure is probably associated with excesssive vasoconstriction and may predispose to damage to internal organs. The relief of pain by drugs may be beneficial as well as humane by changing the pattern of circulatory redistribution to one that is more beneficial to the organism as a whole. In the presence of a decreased blood volume the liability to collapse following movement for transport, diagnosis or treatment, may be modified by gentleness, splintage and by the use of local anæsthesia given, e.g. by injection in a fracture hæmatoma. There may well be a real basis in clinical observation for the thesis of Crile ("Anoci-Association," 1920). When oligæmia is adequately treated by transfusion these risks are minimized.

Anæsthesia. Almost all anæsthetics with the exception of local analgesia, exercise an effect on the circulation which in the presence of oligæmia may lead to dangerous collapse. When oligæmia is fully treated the dangers of anæsthesia for the surgery of moderate injuries are greatly reduced

TREATMENT

First-Aid

In severe injuries the most important duty of those concerned with first-aid is usually to organize the speediest possible removal to hospital combined with the maximum of gentleness in handling at all stages. Except in the presence of certain specific complications, first-aid does not provide any direct "treatment for shock" but rather helps to prevent the action of a number of factors which can make things worse.

The more complicated and the more serious the injury, the more urgent is it to arrange transfer to hospital where there are full facilities for modern treatment of major injuries. In outlying areas, and for certain injuries—particularly in this country in the coal mines—there may be a place for considering the use of blood or blood substitutes during the course of transfer to hospital when this is likely to take more than an hour.

Recent evidence has revealed that the chief risk from anæsthetics in acute injuries is the aspiration of stomach contents when an anaesthetic is given too soon after any kind of a meal. For this reason no patient who may require surgery or anæsthesia for any

injury should ever be given anything by mouth. The traditional hot sweet tea should be confined to those patients who have been shaken up but have obviously not sustained any important injury.

There is no place for any artificial heating in the first-aid treatment of the injured. An ordinary warm blanket may make a patient more comfortable but hot water bottles or hot cradles are never indicated. All movements should be carried out as gently and steadily as possible. The patient should be left alone as much as possible until he can be transferred to a stretcher. If there are signs of severe hæmorrhagic shock the legs should be raised so that the blood can drain down towards the head. Obvious fractures should be splinted, wounds should be covered and bandaged without any attempt at other local treatment. Severe bleeding can nearly always be stopped by firm bandaging over gauze or wool. Tourniquets are very, very seldom of any use. If severe hæmorrhage cannot be stopped without the application of a tourniquet and the patient is not in a desperate condition, the tourniquet can advisably be released a few minutes after firm bandaging of the wound. Urgent action at the first-aid level is required only for:

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transient unconsciousness predispose to such oversights. Fractures of the pelvis, ribs, and spine, ruptures of the spleen and bladder may lead to no complaints and be unassociated with any physical signs on repeated careful examination. Detention for observation may be indicated by mere suspicion while pallor or a transient low blood pressure may give the only clue to an injury that would be lethal if neglected.

The purpose of primary examination is not only to ascertain the extent of the injuries but to assist in the assessment of blood loss. This requires consideration of the nature and history of the injury, the presence of blood on dressings, clothes, floor, stretcher, etc., the size of swellings and X-ray evidence of fractures and knowledge of the degree of blood loss likely to be associated with a given type of injury. The patient's clinical condition may give a clear indication of major bleeding but absence of a clinical picture of shock does not exclude severe internal bleeding. When in doubt frequent observations of the pulse rate and blood pressure are valuable and the sudden development of pallor or sweating may indicate the occurrence of fresh bleeding.

When the injuries indicate a probable blood loss of more than 20–30 per cent it is important to assess the probable duration of oligæmia particularly when a patient arrives in a state of circulatory collapse after a journey or after an interval of an hour or longer. Patients seen within half an hour of injury may with safety wait for transfusion unless the blood pressure is low or bleeding obviously progressive whilst if it is suspected that a low blood volume may have been present for an hour or more transfusion is urgent.

In the presence of major injuries and at times even before examination has been completed, consideration must be given to the need for early surgery. Progressive bleeding from open wounds or into the abdominal cavity will not wait. Surgical treatment for open wounds and fractures, for suspected abdominal lesions, etc., can wait for an attempt at full resuscitation and more detailed assessment. Severe wounds involving muscle require attention within 2–3 hours even when full transfusion facilities are available. Many patients with single or multiple injuries require surgery of a rather less urgent character. The decision must be made if the optimal time for operation is early, as to whether the patient's general condition with treatment will allow such surgery with safety during the first few hours or whether it must be deferred until the patient's general condition is better.

These considerations are an essential part of the estimation that determines treatment designed to prevent or cure "traumatic shock" and the associated features of the *Illness of Trauma.*

Differential Diagnosis

The common need is to decide on the extent of injury and the nature of any resulting collapse. Occasionally traumatic shock may be confused with other conditions which are not necessarily traumatic in origin. The collapse may happen spontaneously and minor or major trauma be added by the resultant fall.

Anaphylactic Shock may be clinically indistinguishable from the direct effect of injury. A history of a recent injection and the absence of other evidence of major injury should provide the necessary clues.

Poisoning from drugs, fumes, or carbon-monoxide is frequently associated with trauma in suicides, burning incidents and explosions. The history of the injury is of vital importance. Poisoning may also result from the ill-advised use of morphia.

Medical Conditions. When minor trauma is super-added or even when a degree of coma interferes with a clear history, it is easy to confuse a number of acute medical emergencies with traumatic shock, in particular—coronary thrombosis, cerebral thrombosis, perforated peptic ulcer, heat-stroke and exhaustion from starvation. A full history from onlookers and careful examination are required.

Cerebral Fat Embolism may complicate trauma. It appears after an interval of hours or days. Pulmonary signs may precede cerebral signs. The diagnosis needs to be borne in mind, although in the absence of the typical rash it is difficult to prove except at autopsy.

Position

Patients in a state of established oligæmic shock with a low blood pressure and a poor pulse, benefit from the head down position.

Splintage

Fractures of the major long bones, especially the femur, require splintage as soon as possible after admission especially when the patient is in pain from their instability and movement.

Oxygen

In the absence of respiratory obstruction or cyanosis, oxygen is rarely of decisive value in the treatment of oligæmic shock.

Morphia

In the presence of pain, severe anxiety or distress, morphia and allied drugs undoubtedly play a part in the treatment of the severely injured patient. They are not to be regarded as "treatment for shock." In the presence of "collapse" with little blood circulating through the skin it is unwise to give morphia hypodermically, especially in large or repeated doses. It may not be absorbed until the circulation is restored. Its action may be delayed and with repeated doses becomes cumulative so that the patient develops morphia poisoning in addition to the effects of injury. It is best given intravenously in small doses ($\frac{1}{6}$ gr.) repeated if necessary according to the result obtained.

Wound Cover and Arrest of Bleeding

Many injured patients are allowed to deteriorate during the period of observation and assessment by oozing from wounds which have been overlooked or neglected. All wounds should be covered with adequate dressings and pressure applied to prevent oozing. Briskly bleeding wounds of the hands or scalp may sometimes be provisionally sutured early, to control bleeding while the patient is got fit for definitive surgery. No attempt should be made to control deep bleeding with artery forceps. It is likely to damage main vessels and may interfere with the possibility of vascular suture.

Early arrest of hæmorrhage is advisable whenever its presence is recognized. Surgery frequently plays a decisive rôle in the resuscitation processes when it facilitates control of deep-seated bleeding.

Temperature

It has been traditional to recommend heat as part of the treatment of shock following trauma. This is based partly on the fact that patients' extremities feel cold and that

in an advanced state of shock the body temperature may be reduced. In fact the cooling of the skin associated with redistribution of blood supply, with or without oligæmia, does not necessarily indicate any reduction of the internal temperature. The insulation may cause an increase in the temperature as recorded high in the rectum. In the presence of oligæmia, heat which succeeds in warming the skin may divert circulating fluid from more essential organs. It can lead to sweating and further fluid loss and in any case is likely to increase the metabolic needs of the tissues. Artificial heating with hot cradles and hot water bottles is likely to produce burns, particularly in the shocked or unconscious patient. Such treatment interferes with observation of skin temperature as a method of assessing the clinical state of the patient. This is of even greater importance in the presence of any threat to the circulation of a limb.

Hot cradles and hot water bottles are absolutely contra-indicated at all stages of the treatment of hæmorrhage and shock. A patient who feels cold may benefit by protection from a blanket, but blankets are warm in themselves and do not require artificial heating.

In hospital the severely injured patient should be looked after at a temperature not above 70°F. Excessive covering with blankets is contra-indicated and in hot weather may be extremely dangerous. The rôle of cooling as a method of treatment is discussed below.

Blood Transfusion

Indications. The most important single measure of proved value in the resuscitation of patients suffering from hæmorrhage and trauma is transfusion. Where whole blood has been lost, replacement by stored whole blood is the treatment of choice. Blood transfusion is no longer to be regarded as a last resort. Its rôle needs consideration under a number of headings:

(1) Resuscitation of patients with severe blood loss. Transfusion is required urgently and rapidly whenever it is suspected that blood loss has occurred to the extent of 30–50 per cent of total blood volume.

(2) In less severe conditions of hæmorrhage and trauma, transfusion is required to prevent the effects of prolonged oligæmia, to prevent the occurrence or development of clinical states of shock and to permit full diagnosis and treatment.

(3) In patients suffering from moderate injuries and blood loss, transfusion is required to prevent complications arising from further blood loss or trauma, to facilitate early definitive surgery and to make anæsthesia safer.

Young fit patients can stand a loss of 1–3 pints ($\frac{1}{2}$–$1\frac{1}{2}$ litres) provided that major surgery is not required and there are no other factors likely to contribute to a state of illness. Greater degrees of hæmorrhage require treatment in all patients, and even lesser degrees of hæmorrhage are worth correction by transfusion in patients who are elderly or suffering from disease likely to be made worse by bleeding.

(4) Transfusion is required to prevent many of the complications of the "illness of trauma," particularly in the presence of major wounds or any predisposition to infection.

In the past it has been suggested that transfusion should be continued until the patients' clinical state has reached some predetermined level of normality, e.g. blood pressure greater than 100, pulse rate 100 or less. Alternatively it has been advocated that transfusion should be continued until it is assessed that the blood volume has reached the level of 80 per cent of normal. Whilst it is true that these indications may sometimes be

adequate, it must be realized that hæmorrhage usually continues during and after operation and that even if it is aimed to secure 100 per cent replacement of early blood loss, the patient may subsequently become seriously anæmic as a result of further hæmorrhage. The majority of patients requiring transfusion will benefit if it is aimed to replace all blood loss by whole blood transfusion and to continue the transfusion to cover further bleeding during the immediate post-operative phase.

The chief limiting factor in relation to such a policy is the availability of blood and laboratory facilities for accurate and rapid grouping and crossmatching. When there is a shortage of blood or a deficiency in laboratory facilities, transfusion indications need to be adapted to the particular situation. The risks of transfusion in any particular set of circumstances must be balanced against its advantages.

Grouping and Crossmatching. Whenever possible, even in acute injuries, blood loss should be replaced by transfusion of type specific blood. Grouping must consider the Rhesus factors in addition to the ABO groups. Modern methods of assessing blood loss from the extent of injury frequently enable us to predict the amount of blood likely to be needed so that transfusion with Group O blood or with blood that has not been fully crossmatched is rarely necessary.

There are patients who require transfusion immediately they are seen and this must be done with ungrouped Group O blood, preferably Rhesus negative. If it is possible to wait for 15–30 minutes, it will probably be possible to use blood of the right group. After a further short delay it should be possible to have a provisional crossmatch and within 2 hours a full crossmatch can be accurately completed by a fully organized laboratory. Even when Group O blood is used to begin with, transfusion can be continued with group-specific blood and finally with blood that has been fully crossmatched.

With such a policy the risk of transfusion should be of the same order as the risk of anæsthesia for minor operations. The major risk from an incompatible transfusion is of renal failure. Renal anoxia from a decreased blood flow due to oligæmia contributes to the risk of renal failure following an incompatible transfusion. The early ending of any state of oligæmia by full transfusion is the best treatment for a single incompatible transfusion. "The treatment of an incompatible transfusion is the continuation of a compatible transfusion at the earliest possible minute."

The other dangers of transfusion; infection, thrombosis, allergic reactions and air embolism can be minimized by careful preparation of transfusion apparatus and materials and attention to detail in technique and observation. The use of air pressure to increase the speed of transfusion should never be carried out without the presence of a responsible medical attendant. Every patient receiving a transfusion should have the first urine specimen passed after transfusion investigated for evidence of a hæmolytic reaction.

With the increasing use of massive transfusions, it has been suggested that the anti-coagulant solutions used for storage may contribute to the danger, either by producing an alteration in the clotting mechanism or by the direct action of a large dose of citrate on the coronary and pulmonary circulations.

Methods of Transfusion. In the majority of patients effective transfusion can be carried out intravenously using a Guest canula. Speed of flow may be accelerated by gravity for which an extendable drip stand is useful. Where this is inadequate the rate of flow may be increased by air pressure with bellows and a sterilized connection containing a filter of cotton wool, or alternatively by means of a rotary pump.

It is sometimes necessary to transfuse into veins of several limbs simultaneously. Occasionally it is necessary to use the femoral vein or the cephalic vein at the shoulder.

Retrograde intra-arterial transfusion may occasionally be a lifesaving measure in patients who are in extremis. In acute trauma arterial transfusion is rarely more effective than intravenous transfusion, although arterial transfusion can be efficiently carried out with a needle inserted into the aorta from the lumbar region.

Rate of Transfusion. In severe oligæmic shock and in patients with moderate recent bleeding, the sooner the blood volume is replaced the better. A pint (500 cc.) of blood can be safely given in 4 minutes, and this rate continued until the blood volume has been restored nearly to normal. Subsequently the rate of transfusion should be slowed down from a continuous stream to a fast drip to cover further bleeding and restore the red cell quota. In patients who have bled slowly over a period of hours so that blood volume has been partially restored by hæmodilution, transfusion should be carried out more cautiously. This is particularly important in elderly patients and in patients with any cardiac abnormality or predisposition to pulmonary œdema. The earlier after hæmorrhage the transfusion is started, the faster can replacement to a normal blood volume be carried out. Any suggestion of developing pulmonary œdema or persistent venous engorgement is an indication to slow down the transfusion.

The rate of transfusion at the acute stage of injury is based on completely different considerations from any transfusion given for anæmia where much greater caution is required. Total quantity of blood required will be based in the first place on the extent of injuries, secondly on the clinical state of the patient and his response to treatment, thirdly on direct control by blood volume studies when they are available. In retrospect transfusion adequacy can be checked by serial hæmoglobin determinations.

Emphasis is placed here on the treatment of oligæmia due to whole blood loss by transfusion with whole blood. When clinical criteria suggest that oligæmia is due to loss of other fluid, the transfusing medium must be modified accordingly.

Plasma*

On the basis of animal experiments it was thought some years ago that plasma or serum could replace whole blood in the treatment of traumatic shock. Moreover pooled plasma can be prepared as a freeze-dried powder which does not require special storage conditions and can be used regardless of the blood group of the recipient. For these reasons plasma was widely introduced early in the 1939–45 War. While satisfactory results were obtained in some cases, in others there was a strong clinical impression that whole blood was more effective and as this became increasingly available in later campaigns, plasma was used to a decreasing extent. A further reason for this was that serious outbreaks of jaundice transmitted by transfusion of plasma had occurred, and in some of these outbreaks the mortality was high. Since the war, alternative methods of preparation of dried plasma have greatly reduced this risk. The latest service of small-pool plasma in Great Britain reveals an incidence of jaundice of the same order as that from whole blood itself. In the United States, recent claims have been made that storage of plasma at room temperature also virtually eliminates the risk of plasma jaundice. The rôle of

* *The sections on "Plasma" and "Plasma substitutes" were contributed by:*
J. P. Bull, M.A., M.D., Director Medical Research Council Industrial Injuries and Burns Research Unit, Birmingham Accident Hospital

plasma in the treatment of shock is still ambiguous, though there seems every reason to give correctly matched whole blood in preference to plasma in cases of blood loss. In conditions such as severe burns, where the loss is primarily of plasma, therapy with plasma is satisfactory, and plasma may be valuable where there is delay in starting a blood transfusion. It should be remembered that the freeze-dried product, though very similar to fluid plasma, is not identical with it, since it contains the extra sodium and citrate ions present in the bottled blood from which it is prepared and may also contain rather high levels of potassium, though this does not seem of great importance in its practical use. When plasma or plasma substitutes are given to patients who already have a normal circulatory volume, the materials are rapidly lost from the circulation, but when there is a circulatory volume deficit, they can play a part in maintaining circulatory volume until it is reconstituted with its normal constituents.

Plasma Substitutes

For 40 years or more attempts have been made to devise transfusion fluids which will substitute for natural blood products. It would obviously be convenient to have a solution which could be prepared commercially in any quantities which might be needed, without the inconvenience of requiring blood donors. Such materials would have the further advantage of freedom from risk of transmitting jaundice. Since it is not possible in the forseeable future to make any substitute for red cells, the aim at present is rather to provide a colloidal solution which may be used in place of plasma.

Desirable properties of such plasma substitutes may be listed as follows:

Positive qualities:

(*a*) Colloid osmotic pressure and viscosity similar to plasma.
(*b*) Retention in circulation until replaced by normal plasma proteins.
(*c*) Constant composition between batches.
(*d*) Stability in storage and sterilization.
(*e*) Should be fluid at temperatures above 0°C.

Negative qualities:

(*a*) Non-antigenic.
(*b*) Non-toxic locally or generally.
(*c*) Should not affect agglutination or coagulation of blood.

Substances which can theoretically fulfil these requirements and are therefore eligible as substitutes include non-antigenic proteins, naturally occurring polysaccharides and synthetic macromolecules. Gelatin was the first substance to be tried for this purpose, and various solutions of gelatin and of derivatives such as oxypolygel have had their supporters for many years. The gelatin molecule is not antigenic and can be metabolized as a protein food, but the molecules are smaller than those of plasma proteins and the material is soon lost from the circulation. Another difficulty is that if the molecules are made larger, the solutions are no longer fluid at room temperature. During the First World War solutions of gum arabic were shown to be effective in replacing the circulatory volume of animals and injured men. The molecules—naturally occurring polysaccharides—were never closely defined chemically, and were subject to variation due to their vegetable origin. After some years of use, evidence accumulated of liver damage

following the use of gum saline solutions, and it is no longer considered safe for clinical use.

During the Second World War, a synthetic colloid, polyvinyl pyrrolidone (PVP) was used extensively by the Germans as a transfusion material. This substance can be prepared of known composition and molecular size. It appears that no metabolism of this compound can occur in the body; this means that if the molecules are to be large enough to give a sustained maintenance of circulatory volume they are liable to be stored for very long periods in the body, though it is not clear that any harmful effects result. In practice, the solutions offered commercially have molecules which are mostly smaller than this and are therefore soon excreted by the kidneys. The corollary of this is that the maintenance of circulatory volume is not sustained for a long period. Probably the most satisfactory plasma substitute to date is a solution of dextran. This is a polysaccharide produced by a fermentation process which can be prepared to have a range of molecular size very similar to that of plasma proteins. Slow metabolism of the dextran probably occurs so that material which becomes temporarily stored in tissues is gradually broken down.

In recent years there have been extensive experimental and clinical trials of both PVP and dextran. It is clear that both substitutes are reasonably free from toxic effects, and that they produce the expected expansion of circulatory volume when transfused. As would be expected, the concentration of the substance in the circulation depends upon the amount and rate of administration, and the plasma protein level is correspondingly depressed. The total colloid concentration in the plasma tends to remain constant. The level of foreign colloid gradually diminishes as it is lost from the circulation, either into the tissues or via the kidneys. In the case of dextran, the plasma level falls by about one-third per day. *Corresponding to this fall, the plasma protein rises again to normal* values. Since these materials are foreign to the body, it is reasonable not to give very large quantities, so as to minimize storage effects. The rapid loss of PVP from the body implies that this material can only be expected to have a temporary supporting rôle, as *for instance while awaiting blood transfusion to be started. Larger molecules of dextran* make it eligible as a definitive substitute for plasma, and encouraging results have been reported in the treatment of burns, where the main requirement is for plasma rather than whole blood. In moderately severe burns shock, dextran alone may be adequate; in other cases, combination with plasma and/or blood is probably preferable. If red cells have been lost, whole blood is the appropriate treatment rather than either plasma or plasma substitutes. All effective plasma substitutes cause dilution of normal blood constituents, and though this seems to be tolerable in moderate degree, it is preferable that transfusion with substitutes should be limited in quantity. It has been suggested that the maximum of one plasma volume of dextran (i e. 3 litres in an adult) is a reasonable limit, though cases have been successfully treated with larger amounts when blood or plasma has not been available. Certain undesirable reactions to dextran have been reported. When given to normal volunteers, a proportion of cases show an allergic response, but this seems of little or no importance in clinical cases since several large series have been reported with substantial freedom from reactions. Another finding after dextran has been that in some cases bleeding time is prolonged. This is not yet fully understood, and does not appear to be of great clinical importance but should be borne in mind when patients receiving dextran are being operated upon while the dextran level in the blood is still high.

Hibernation and Cooling

It has recently been suggested that a considerable part of the clinical state of patients suffering from major injuries can be attributed to exaggerated and "unnecessary" reactions which can be controlled by inducing a state of "artificial hibernation" (Laborit and Hugenard, 1956). The state of so-called "hibernation" is induced with the aid of the "lytic cocktail," the chief constituent of which is chlorpromazine or one of the more recent drugs of this type. These drugs alone or in combination with surface cooling are claimed to reduce the metabolic needs of the organism and to allow the vegetative nervous system to take control so that exaggerated and inappropriate reactions are minimized. It has not yet been established that this method of treatment is either safe or desirable in acute trauma as a routine part of the handling of major injuries.

Meanwhile chlorpromazine has been shown to be a useful adjunct to premedication and "facilitates" the use of other anæsthetic agents. Cooling has made an important contribution to deliberate cardiac surgery. There is evidence to suggest that it can be valuable in the treatment of severe head injuries and severe infections. The rôle of cooling or hibernation in traumatic shock requires much more detailed knowledge of the nervous and metabolic responses to trauma and its treatment by more orthodox measures.

Noradrenaline and Cortisone

Many attempts have been made to restore the blood pressure in oligæmic shock by the use of vasoconstrictor drugs. The latest of these, Noradrenaline, may occasionally be useful where patients do not recover their normal vascular tone following adequate transfusion. Most of the patients in whom it is claimed that Noradrenaline has been decisive in treatment have in fact been transfused too late or too slowly. In the presence of moderate hæmorrhage and a state of vasoconstriction, Noradrenaline is likely to do more harm than good. Its use in conditions known to be due to a decrease in vasomotor tone, e.g. collapse following spinal injuries, is more logical although the same effect has been obtained in the past with ephedrine. It is suggested on experimental grounds that Noradrenaline is less likely to produce vasoconstriction of the renal vessels.

Considerable interest has been focused in recent years on the pituitary and suprarenal cortex. The "stress reaction" of Selye does not adequately describe all the phenomena associated with the general response to injury. The action of the endocrine system is closely linked with that of the nervous system as a whole. It is only rarely possible to conclude that an individual is suffering from "exhaustion" of the suprarenal cortex. The majority of patients in the acute stage of injury show evidence of increased secretion of cortico-steroids and cortisone is probably contra-indicated in the early stages of all severe injuries. Its use should be restricted to patients with late metabolic or circulatory disturbances following injury when there is evidence of adreno-cortical failure. This may occasionally result from direct injury to the suprarenal glands.

CRUSH SYNDROME—TRAUMATIC ANURIA

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necessary space and facilities, and this is only possible in hospitals or departments specifically organized for the reception and treatment of injuries.

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The condition was further investigated by Bywaters and others (1941) during the aerial bombardment of London in 1940-41. Patients whose limbs had been crushed or compressed under fallen masonry for long periods were found subsequently to develop renal failure and a characteristic pathological condition of the kidneys. It was accepted for a time that this was due to the action of myohæmoglobin or a derivative of this substance liberated from the crushed muscles and acting on the distal tubule of the kidney to produce tubular necrosis. Subsequently it emerged that myohæmoglobin could be found in the urine and kidneys of many patients who died with severe muscle injury, particularly battle casualties, even in the absence of renal failure. Further investigation has shown that many patients who recover from major wounds develop some degree of renal damage and it is now accepted that the most important factor contributing to the development of renal failure following injury of all types is loss of blood or other fluid into the injured tissues and the resultant oligæmia. Persistent oligæmia is associated with a reduction in the blood supply to the kidney, and the duration of this is probably decisive.

Many of the patients described as typical of "crush syndrome" have lost enormous quantities of fluid into the limbs even though the injury has resulted in little frank hæmorrhage into the tissues. The extent of fluid loss and the resulting prolonged low blood volume has not in the past been fully appreciated. It is possible that myohæmoglobin or other products derived from damaged tissues provide an added irritation or physical obstruction to a kidney whose viability is already interfered with by anoxia and diminution of arterial blood flow.

During the Second World War when surgeons were beginning to appreciate the necessity for adequate transfusion, many patients survived their primary injury and operation with the aid of transfusion sufficient to deal with the immediate state of shock but insufficient to restore the blood supply to the kidney in time. With the further development of our knowledge of transfusion needs, the frequency of traumatic anuria in patients with injuries of similar severity has decreased considerably. It remains a major problem in burns and in very severe battle casualties.

The most important measure that can be taken to prevent the onset of traumatic anuria following injury of any kind is early adequate transfusion. As soon as the presence of renal failure is indicated by a fall in renal output no attempt should be made to "stimulate" renal function, but rather attention should be paid to sparing the affected kidney by withholding protein, providing calories as carbohydrates and limiting the intake of water. In the absence of severe tissue damage many injuries have recovered following the institution of such a regime (Bull, *et al*, 1949). When conservative treatment fails the use of an artificial kidney may be indicated.

CONCLUSION

Whatever theoretical approach may be adopted to the balance of factors acting in a given injured patient, whatever general approach to treatment is adopted, one thing is becoming increasingly evident: the prevention and treatment of the systemic response to injury requires the continuous supervision of experienced medical and surgical staff from the time of admission to hospital until recovery is assured. The medical team requires a full service of laboratory, radiological, and nursing assistance with the

penicillin had been discovered (by Fleming in 1928), but it was not obtained in a therapeutically useful form until the early years of the Second World War, when the Oxford workers under Florey developed an effective process of extraction. The success of penicillin stimulated intensive search on both sides of the Atlantic for similar antibiotics produced by moulds, bacteria and higher organisms. From countless specimens examined a relatively small number of agents has been derived which fulfil the requirements for chemotherapeutic use. The most important of these are streptomycin, the tetracyclines, chloramphenicol, erythromycin, polymyxin, neomycin, bacitracin, and most recently novobiocin. A few synthetic agents of comparable importance have been introduced during this period, notably isoniazid, para-aminosalicylic acid and the newer sulphonamides; but living organisms have, on the whole, proved a more useful source of new chemotherapeutic agents than the chemical laboratory.

The distinction between antibiotics and other chemotherapeutic agents is of no clinical importance. Several of the former are of known chemical structure, and one of them (chloramphenicol) is produced commercially by a synthetic process. It is appropriate, therefore, to refer to them all as chemotherapeutic agents until a simpler collective term is introduced. A more important distinction is that between bactericidal and predominantly bacteriostatic drugs, since the two may interfere with each others' activity; further details about this are presented below (see *Methods of Administration*).

Chemotherapeutic agents are further distinguished by their range of action (or "spectrum"), by their routes of administration, by their absorption from the alimentary canal, by their toxicity, and by the readiness with which resistant bacteria emerge in patients under treatment. Some of them (e.g. neomycin and bacitracin) are too toxic for systemic use, except in grave emergencies, but may be valuable on local application; it would perhaps be more appropriate to classify these agents as antiseptics.

Each of the agents described below (see also Tables I and II) has a selective action against a range of pathogenic organisms at concentrations which are relatively free from toxicity to the patient or to his tissues; such action is not appreciably reduced in the presence of blood or of exudates. Only compounds which possess these features are considered eligible for use as chemotherapeutic agents.

The Sulphonamides.[1,2] "Prontosil" (sulphonamido-crysoidin) cured streptococcal infection of mice, but was inactive against streptococci *in vitro*. The therapeutic effect was found to be due to sulphanilamide, which in the body is liberated from its attachment to crysoidin. A series of related compounds, the sulphonamides, was synthesized and found active against a wide range of organisms. Streptococci and pneumococci were shown to be particularly sensitive, but many other organisms were inhibited by sulphonamides, notably *Staph. aureus* and members of the coli-typhoid-dysentery group. Sulphonamides inhibit the metabolism of p-amino benzoic acid, an essential growth factor for many bacteria, and their action is predominantly bacteriostatic.

Although the sulphonamides have been overshadowed by antibiotics, they still have an important place in chemotherapy. In particular, their ability to pass the "blood-brain barrier" makes them still the drugs of choice in meningitis due to sensitive organisms (especially meningococci). Resistant strains of streptococci, staphylococci and other bacteria are common, and may emerge under treatment. There is cross-resistance between the different sulphonamides, but the more active members may retain some activity against an organism which grows readily in the presence of less active compounds.

CHAPTER XV

CHEMOTHERAPY IN SURGERY

E. J. L. LOWBURY

THE application of chemotherapy (including the antibiotics) in the field of surgery is an advance of historic importance, perhaps the greatest since the establishment of the principles of asepsis. It has contributed towards (1) the prevention and treatment of infection following surgical operations; (2) the prevention and treatment of infection complicating accidental wounds; (3) the treatment of established infective lesions; and (4) more definitive surgery, particularly in the resection of infected tissues. Chemotherapy has given the surgeon weapons to use against bacteria which may break through the aseptic barrier, and has strengthened that barrier against some of the more dangerous pathogens; in this field a major victory has been scored over *Streptococcus pyogenes*, one of the commonest and most dangerous aerobic wound pathogens in the days before the advent of the sulphonamides and penicillin. Certain infections for which operation was formerly required may often be cured today by systemic chemotherapy. At the same time chemotherapy, combined with other advances (e.g. in blood transfusion and control of fluid and electrolyte balance), has greatly widened the scope of operative surgery.

Unfortunately, these benefits are to some extent offset by the problems which have arisen through the emergence of resistant bacteria, especially staphylococci, and the enthusiasm which was general at the beginning of the penicillin era has been followed by a period of doubt and uncertainty. For this reason, and also because of the increasing experience of toxicity and sensitization, there is a reaction against uncritical reliance on chemotherapy at the expense of asepsis and the older principles of treatment. Meanwhile the field of chemotherapy is developing rapidly, and any survey of current knowledge is likely to be out of date in a short time. The clinical assessment of chemotherapy, especially in surgery, has been incomplete and frequently uncontrolled. It is therefore rarely possible to be dogmatic about the treatment of a particular infection or threatened infection, although appropriate agents may be selected from the extensive range now available. In the pages that follow we shall consider this range of chemotherapeutic agents and their use in various fields of surgery; we shall discuss the emergence of resistant bacteria and the methods which have been suggested to deal with this problem.

Antibiotics and Other Chemotherapeutic Agents

Antiseptics were originally used for the treatment and prophylaxis of wound infections, and modern surgery owes its origin to the development of this method by Lister. On account of their toxicity, however, these compounds could not be administered, by mouth or by injection, for the systemic treatment of infectious disease. Chemotherapy began when Ehrlich found that it was possible to use certain organic arsenicals and synthetic dyes in this way with comparative safety for the treatment of syphilis and trypanosomiasis. *Work which began before the First World War culminated, in 1935, with Domagk's* synthesis of "prontosil," the first therapeutically successful sulphonamide. By that time

strains of *Staph. aureus* and Gram negative bacilli, are resistant to penicillin through the production of penicillinase, which in a mixed infection (e.g. of a wound) may protect sensitive organisms (e.g. *Strep. pyogenes*) against the effects of penicillin therapy.

The Preparations. A number of different penicillins are produced by *Penicillium notatum* and *Penicillium chrysogenum*. These have been described as penicillin and dihydropenicillin F, and penicillin G, X, K, and V. The related compounds, cephalosporin B, N, and P, with different spectra, are still under investigation. Penicillin G (benzyl penicillin) and penicillin V (phenoxymethyl penicillin) provide the most satisfactory clinical preparations, the latter being stable in the presence of gastric secretions, and therefore suitable for oral administration.[7,8,9]

Many commercial preparations of penicillin are available. They may be classified as follows: (1) Penicillin G, usually in the form of the sodium or potassium salt; primarily for injection. Preparations with added sulphonamide or streptomycin can be obtained. (2) Penicillin ester[10,11] (the hydriodide of diethylamino-ethanol ester of penicillin G), which has affinities for lung and for nerve tissues. (3) Repository penicillins: (*a*) procaine penicillin, (*b*) benethamine penicillin,[12,13] and (*c*) benzathine penicillin.[14] These (especially (*b*) and (*c*)) are absorbed slowly into the blood stream after injection Therapeutic levels of penicillin persist in the blood for as long as 7 days after a single intramuscular injection of benzathine penicillin. (4) Oral penicillin: the earlier forms of oral penicillin have been superseded by penicillin V. (5) Creams, ointments, powders, eyedrops, solutions and other preparations for local use

Administration and Dosage. When high blood levels are required, penicillin G should be given by intramuscular or, if necessary, by intravenous injection (e.g. 500,000 units 12 hourly, or sometimes more frequently). The blood level may be further raised and kept high by giving 2 grams of "benemid" daily. For less severe infections, for outpatients and for prophylaxis, repository penicillins are useful; oral penicillin (e.g. penicillin V, 375 mg. daily) is a convenient alternative, especially for children.

Penicillin diffuses readily through the tissues and appears in effective concentration in synovial, peritoneal and pleural exudates. Unlike sulphonamides, however, it does not pass readily into the cerebrospinal fluid. In the treatment of meningitis with organisms sensitive to penicillin and resistant to sulphonamides, intramuscular penicillin should be given in very high dosage (e g. 1 million units 2 hourly). The advantage of additional intrathecal injections is doubtful, and severe reactions may follow such treatment.

Penicillin creams and powders containing 1,000–10,000 units per gram have been found useful in the treatment of burns (see below).

Toxicity. An increasing incidence of sensitization, including severe dermatitis and, occasionally, anaphylaxis, has been reported in recent years.[15,16] Other forms of toxic action are meningeal irritation following intrathecal injection, and local pain during intramuscular injection.

The "Broad Spectrum" Antibiotics. This term is applied to chloramphenicol and the tetracyclines, which are active against a wide range of Gram positive and Gram negative organisms, and also against certain Rickettsiæ and larger viruses.

CHLORAMPHENICOL[17,5] ("Chloromycetin," "Alficetyn"). Originally obtained from the culture of *Streptomyces venezuelæ* in 1947, chloramphenicol was soon defined chemically and produced by a synthetic process. It is very sparingly soluble in water (0·25 g. per 100 ml.), but more soluble in some organic solvents (e.g. propylene glycol and ethyl

The Preparations. Sulphadimidine ("sulphamezathine") is probably the best of the sulphonamides for routine use. It is more rapidly and completely absorbed, reaches a higher level in the blood, is more slowly excreted and more soluble in acid urine than *sulphadiazine*. Sulphadiazine, however, is slightly more active and probably the drug of choice in the treatment of meningitis. "*Sulphatriad*" a mixture of sulphathiazole, sulphadiazine and sulphamerazine) may be used as an alternative for sulphadimidine. The earlier sulphonamides, *sulphanilamide* and *sulphapyridine*, are less active and more toxic, and there are no special indications for their retention. *Sulphacetamide* is a highly soluble neutral salt used in eye drops. The poorly absorbed sulphonamides, *succinyl sulphathiazole, phthalylsulphathiazole* and *sulphaguanidine*, are suitable for the treatment of dysentery and before operations on the colon; the first of these is probably the most useful.

Administration and Dosage. Sulphadimidine, sulphathiazole and sulphadiazine are well absorbed from the intestine. The adult dosage for most purposes is 1·0 gm. every six hours, beginning with a "loading dose" of 3·0 gm., and continuing at full dosage for 7 days. This dosage may be halved for urinary infections as the drug is concentrated in the urine. When sulphadiazine or sulphathiazole are given, the urine should be kept alkaline with a mixture containing equal parts of potassium citrate and sodium bicarbonate, and 5 or 6 pints of fluid should be taken daily. For very severe or fulminating infections the "loading dose" of sulphadiazine should be given intravenously. Sulphacetamide sodium eye drops are generally made up as a 10 per cent solution, and instilled every 2 hours.

Toxicity. Drug fever, often accompanied by a maculo-papular rash, is a common side effect, appearing as the result of sensitization on or after the fifth day of treatment. Slight malaise or anorexia are common. Other side-effects are rare if the drug is used with caution. Hæmaturia, renal colic and occasionally anuria are risks in sulphadiazine or sulphathiazole therapy, but they can be largely prevented by ensuring a daily output of 50 oz. of alkaline urine: the risk of anuria is negligible if sulphadimidine or sulphatriad are given. Blood dyscrasias (agranulocytosis, aplastic anæmia, purpura) are liable to occur only if treatment is continued for more than 10 days or is not stopped on the appearance of an allergic reaction. Methæmoglobinæmia and sulphæmoglobinæmia are very rare side effects. On the appearance of any of these complications (except perhaps methæmoglobinæmia), the course of sulphonamide should be stopped.

Penicillin.[3,4,5,6] Fifteen years after its introduction for clinical use, the first effective antibiotic, penicillin, is still undoubtedly the first in importance. This is due to its freedom from direct toxic effects (though sensitization is now fairly common), and to its powerful bactericidal action against a wide range of organisms, including several of primary concern to the surgeon. This action is not impaired by blood or by pus. The sensitive organisms include ærobic and anærobic streptococci, staphylococci, pneumococci, the clostridia of tetanus and gas gangrene, gonococci and meningococci, *B. anthracis, C. diphtheriæ, Erysipelothrix rhusiopathiæ, Actinomyces israeli*, and the spirochætes of syphilis, Vincent's angina and relapsing fever. The Gram negative bacilli are in varying degrees resistant. The emergence of resistant strains of bacteria usually sensitive varies with the species, but it has proved a problem of clinical importance only in the case of *Staphylococcus aureus* (see below). Resistance of *Streptococcus pyogenes* to penicillin has never been repeatably demonstrated on any strain. Many organisms, including

strains of *Staph. aureus* and Gram negative bacilli, are resistant to penicillin through the production of penicillinase, which in a mixed infection (e.g. of a wound) may protect sensitive organisms (e.g. *Strep. pyogenes*) against the effects of penicillin therapy.

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alcohol). Solutions are stable, and lose little activity on boiling or on autoclaving at low pressure.

Chloramphenicol is predominantly bacteriostatic. The organisms of surgical importance against which it is active include staphylococci, streptococci, clostridia, and Gram negative bacilli (including many strains of Proteus). Resistant strains of *Staph. aureus* occur, and tend to appear in patients under treatment. For most of these organisms (when sensitive) the tetracyclines are as effective and safer; chloramphenicol is still, however, considered to be the best antibiotic for use in the treatment of typhoid fever.

Administration and Dosage. The usual administration is by mouth, two capsules (500 mg.) being given 6 hourly to adults in a course which should, in general, not exceed 7 days An intramuscular preparation is available, to be given at a dosage of 100 mg. per kg. body weight per day. Other preparations are a cream (1 per cent), solution (5 per cent), eardrops (10 per cent), ophthalmic ointment (1 per cent), and eyedrops (0·5 per cent).

Chloramphenicol is absorbed from the gut and diffuses widely through all the tissues and to a greater degree than the other antibiotics passes the blood-brain barrier; it also penetrates to all parts of the eye except the lens, and passes through the placenta. The antibiotic is largely excreted in the urine.

Toxicity. Aplastic anæmia has been reported in a considerable number of patients who have received chloramphenicol, occasionally after a short course of treatment.[18,19] This complication, though rare, is usually fatal, and makes it desirable to reserve the use of chloramphenicol for serious infection which cannot be adequately treated with other agents.

Vomiting and diarrhœa occur much less frequently during treatment with chloramphenicol than with the tetracyclines.

THE TETRACYCLINES.[20,21,5] The three members of this group, chlortetracycline ("Aureomycin"), oxytetracycline ("Terramycin") and tetracycline itself ("Achromycin" or "Tetracyn") are closely related in structure and in activity. Chlortetracycline and oxytetracycline are derived by fermentation processes from different species of streptomyces; tetracycline is obtained by a chemical process from chlortetracycline. All three are marketed as sparingly soluble hydrochlorides. Tetracycline is the most stable and the least toxic of these compounds, while chlortetracycline lies at the other extreme in both respects. The organisms against which the tetracyclines are particularly active correspond roughly with those sensitive to chloramphenicol. *Strep. pyogenes* and *Staph. aureus* are rather more sensitive to the tetracyclines than to chloramphenicol, but tetracycline-resistant variants of the staphylococci are commoner. Like chloramphenicol, the tetracyclines are predominantly bacteriostatic. Cross-resistance of bacteria to the different tetracyclines is almost invariable, but there are minor differences in the response of organisms to the different members of the group (e.g. *Staph. aureus* is slightly more sensitive to chlortetracycline than to the others)

Administration and Dosage. Tetracycline and chlortetracycline are prescribed at the same dosage (usually 250 mg. 6 hourly) and oxytetracycline at twice that dosage. Tetracycline may be given by mouth (as capsules, tablets, or pædiatric fluids), by intravenous infusion (10–20 mg. per kg. per day), by intramuscular injection (3 mg. per kg. per day), and locally as an ointment (3 per cent), an ophthalmic ointment (1 per cent) and as ear drops (0·5 per cent with benzocaine in propylene glycol)

The tetracyclines are fairly well absorbed from the gut and diffuse through the tissues

in much the same way as chloramphenicol, though the C.S.F. levels are less satisfactory. Intravenous tetracycline is probably the best choice if this group of antibiotics is indicated for treatment of meningitis. If the optimum oral dose is exceeded, an excess of the drug is likely to accumulate in the gut and cause irritation.

Toxicity. Nausea, vomiting and diarrhœa commonly occur, especially during treatment with chlortetracycline. These symptoms are apparently due partly to irritation and partly to modification of the gut flora. The latter may also lead to infection of the mouth and the anus with *Candida albicans*, and to pellagra-like changes which are probably due to vitamin B deficiency; more serious consequences are an extension of the Candida infection to the lungs, or an acute and often fatal enterocolitis which is usually due to tetracycline-resistant *Staph. aureus*. To prevent these symptoms, chlortetracycline should, when possible, be avoided, and the drug selected should be swallowed with milk or with a mixture of calcium caseinate and calcium carbonate.[22] Vitamin B complex should also be given. The administration of tetracycline-resistant strains of lactobacilli to replace the gut flora has been suggested, and it is possible that neomycin, which is active against all staphylococci and not absorbed from the gut, would be a useful prophylactic against staphylococcal enterocolitis if taken by mouth together with tetracyclines.

Other toxic effects of tetracyclines which have occasionally been reported are jaundice and sensitization, the latter after local application of the drug.

Erythromycin[23,5] ("Ilotycin," "Erythrocin"). This antibiotic, produced by *Streptomyces erythreus*, is a basic compound, sparingly soluble in water, and relatively stable in solution. It is slightly more active at pH 8 than at pH 7. Its range of action is similar to that of penicillin, but it is also active against *Hæmophilus pertussis* and *Hæmophilus influenzæ*. Its action is predominantly bacteriostatic. Staphylococci readily become resistant when grown in the presence of erythromycin, but resistant strains of *Strep. pyogenes* have not been described.

Carbomycin ("Magnamycin"), spiramycin ("Rovamycin") and oleandomycin ("Matromycin," "Romicil") are antibiotics related in their mode of action to erythromycin; staphylococci rendered resistant to any of these agents are usually found to have acquired resistance to all of them, but there is evidence that resistance acquired *in vivo* to spiramycin and to oleandomycin is more specific.

Administration and Dosage. The drug is readily absorbed from the gut, and is usually given by mouth, as a tablet or a pædiatric preparation, the average adult dose being 300 mg. 6 hourly. It may also be given intravenously as an infusion of 1 mg. per ml. by continuous drip or as intermittent therapy; 1–2 gm. of the antibiotic may be given by this route in 24 hours.

Erythromycin diffuses readily to all tissues except brain and C.S.F. It is highly concentrated in the bile and passes the placental barrier.

Toxicity. Abdominal discomfort and soft stools often occur during erythromycin therapy. No severe toxic effects have been reported.

Novobiocin[24] ("Albamycin"). This antibiotic, which was first described in 1955, is produced by *Streptomyces niveus*, and resembles erythromycin in its range of action. Many Gram-positive organisms, including *Staph. aureus* and *Strep. pyogenes*, are sensitive, but the former readily acquires resistance *in vitro* and in patients under treatment. The action is predominantly bacteriostatic. There is no cross-resistance with erythromycin or with any other agent.

Novobiocin, like penicillin, is an acid, and is manufactured as the sodium salt.

Administration and Dosage. Novobiocin is exceptionally well absorbed from the alimentary canal, equal dosage giving blood levels ten times as high as tetracycline and twenty-five times as high as erythromycin. Appreciable blood levels persist for 8 hours or more. Preparations for intravenous and intramuscular administration are also available for trial. It is found satisfactory to give novobiocin to adults in two daily doses of 500 mg. (2 capsules per dose). The antibiotic penetrates well to all tissues except brain and C.S.F. and is concentrated in the bile.

Toxicity. Sensitization reactions have been found in a number of patients treated with novobiocin.

The Polymyxins.[25,26] Of the five polymyxins, A, B, C, D, and E, two (B and E) are sufficiently free from toxic action to be injected, and of these, only polymyxin B is commercially available. The polymyxins, which were independently discovered in England and in the United States in 1947, are polypeptides produced by *Bacillus polymyxa.* They are "narrow-spectrum" antibiotics, active only against certain Gram-negative bacilli, notably *Ps. pyocyanea.* With very few exceptions, all strains of this organism have been found sensitive to polymyxin and cannot be induced to acquire resistance either *in vitro* or *in vivo*; they are usually resistant or relatively resistant to other antibiotics. *Hæmophilus influenzæ*, shigellæ and salmonellæ are sensitive to polymyxin. Members of the Proteus group are resistant, and the coli-ærogenes group includes both sensitive and resistant strains.

Administration and Dosage. Intramuscular injection of 2·0 to 2·5 mg. per kg. body weight daily (e.g. 100–150 mg., or 1·0–1·5 mega units for an adult) results in a good distribution to the tissues, but not to body cavities, brain and C.S.F. When required for the treatment of meningitis, 2·0–4·0 mg. of polymyxin should be given by intrathecal injection 12-hourly, or 5·0 mg. every 24 hours.

Polymyxin is available as ear drops (1 mg. per ml.) and can be given by subconjunctival injection. Creams and dusting powders containing 1 mg. polymyxin per gram have been found useful in the local treatment of burns.

Toxicity. Patients receiving polymyxin B by intramuscular injection often complain of pain at the site of injection, and sometimes of itching around the mouth and on the scalp. There are also reports of proteinuria, pyrexia, irritability, ataxia, flushing, drowsiness and urticaria; these side-effects, which are rare and apparently transient, are no contraindication to the systemic use of polymyxin B in severe infections with *Ps. pyocyanea.*

Chemotherapeutic Agents for the Treatment of Tuberculosis[5,27]

STREPTOMYCIN. This antibiotic, produced by *Streptomyces griseus,* was first described in 1944. It is a base which forms soluble salts with hydrochloric and sulphuric acids. Solutions are stable. Dihydrostreptomycin is obtained by shaking the trihydrochloride with palladium or platinum in the presence of hydrogen.

Streptomycin is bactericidal towards a wide range of Gram-positive and Gram-negative organisms, but inactive against anærobes. Its activity is optimal at pH 7·8. On account of its potential toxicity and of the rapid emergence under treatment of resistant variants of all sensitive organisms, streptomycin and dihydrostreptomycin are largely reserved to-day for the treatment of tuberculosis, against which the other available antibiotics are ineffective.

Toxicity. If the adult dose is restricted to 1 gm. a day or less, toxic effects are infrequent, and tend to appear only after several weeks of treatment. Streptomycin is liable to damage the vestibular nerve, causing giddiness, nystagmus and nausea and other symptoms which may continue after treatment is stopped. Dihydrostreptomycin is liable to cause irreversible deafness through its action on the auditory nerve. The risks of these side-effects are diminished by giving streptomycin and dihydrostreptomycin together, each at half dose. Other toxic effects recorded are pain on injection, sensitization dermatitis and, more rarely, agranulocytosis, aplastic anæmia, and albuminuria.

PARA-AMINOSALICYLIC ACID (P.A.S.). This compound and its sodium salt were found, in 1946, to have a bacteriostatic action against tubercle bacilli; high dilutions (0·1 to 1·0 μg. per ml.) inhibit growth. The organisms readily acquire resistance.

Toxicity. P.A.S. given by mouth causes alimentary disturbances, including vomiting and diarrhœa, in about 50 per cent of the patients receiving treatment; these symptoms do not occur when the drug is given by subcutaneous or intravenous routes. Severe sensitization, including drug fever and exfoliative dermatitis, headache, conjunctival irritation, lymphadenopathy, cough, jaundice, and potassium deficiency have also been reported as side-effects.

ISONIAZID. Isoniazid is a synthetic compound (isonicotinic acid hydrazide) which was found in 1952 to have a bacteriostatic effect on cultures of tubercle bacilli and related organisms, very high dilutions being active (e.g. 0·02 μg./ml.). Other groups of bacteria are not affected. Resistance is readily acquired by the tubercle bacilli.

Toxicity. Tremor, twitching and restlessness are the commonest toxic effects. Skin rashes, peripheral neuritis and hæmoptysis have been described. When the recommended dosage is not exceeded, toxic effects are usually not found, and when they occur are slight and transient.

ADMINISTRATION AND DOSAGE OF THE ANTI-TUBERCULOUS DRUGS. *Streptomycin.* The antibiotic is not absorbed from the gut, and should be given by intramuscular injection. The adult dose is 1 gm. daily. An effective blood level (25–50 μg./ml.) is reached in one hour after the injection. The antibiotic diffuses readily to all tissues. After prolonged treatment it reaches pleural and peritoneal fluids in concentrations that approach the blood level; there is little penetration to the cerebro-spinal fluid in health, but fairly good concentrations may occur in meningitis. Intrathecal injection (50–100 mg. daily) may be given. Eyedrops are used at a dilution of 0·01 g. in 1 ml. saline. The dose for intrapleural injection is 0·5 g. in 10 ml. water.

Para-aminosalicylic acid is rapidly absorbed from the gut, and is therefore usually given by mouth, the adult dose being 12–20 gm. per day. The drug may also be given by intravenous injection in a drip infusion. When administered in this way, moderate levels of P.A.S. are obtained in the cerebro-spinal fluid, but these may be raised by intrathecal injection of a 0·3 per cent solution.

Isoniazid given by mouth is absorbed rapidly. The adult dosage is 100 mg. 12 hourly (or 1·5 mg. per kg.). The drug diffuses well to all tissues; the C.S.F. level is similar to that of the blood.

In the management of tuberculosis it is important that two of these chemotherapeutic agents should be administered at the same time, in order to prevent, or at least delay, the emergence of resistant strains during treatment. Treatment is continued until signs of infection have disappeared—usually 3–6 months or longer. A careful watch for the

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Streptomycin is bactericidal towards a wide range of Gram-positive and Gram-negative organisms, but inactive against anærobes. Its activity is optimal at pH 7·8. On account of its potential toxicity and of the rapid emergence under treatment of resistant variants of all sensitive organisms, streptomycin and dihydrostreptomycin are largely reserved to-day for the treatment of tuberculosis, against which the other available antibiotics are ineffective.

concentrations can be reached by local application or instillation, and an agent may sometimes be therapeutically effective by this route when it is ineffective by mouth or by injection (e.g. polymyxin against *Ps. pyocyanea* in burns).

Organisms tested for sensitivity to a new agent can be divided into three groups: (1) those of which all strains are resistant; (2) those of which some strains are resistant and some are sensitive; and (3) those of which all strains are sensitive. If the agent is introduced for routine use, especially in a hospital or other institution, the resistant members of group 2 tend to be selected and to become predominant. In addition, certain organisms originally placed in group 3 begin to show resistant members, which are selected in the same way as the resistant strains of group 2. There has been much controversy as to whether these resistant strains emerge (*a*) by mutation from sensitive parent strains, followed by selection; (*b*) by adaptation through contact with the agent, also followed by selection, or (*c*) by selection of resistant organisms normally present in very small numbers. There is evidence to support each of these hypotheses, and the mechanism probably varies with the organisms and the antibiotic, as do the frequency and the nature of resistant variants.

Of the organisms which cause surgical infection, *Streptococcus pyogenes* has been outstandingly vulnerable to the antibiotics. Resistance to the sulphonamides had become fairly common by the time penicillin was introduced, but no penicillin-resistant strains have yet been isolated. Resistance to the tetracyclines, however, is now familiar, especially in the treatment of burns. By contrast with *Strep. pyogenes*, *Staph. aureus* has produced resistant variants against all the agents available for systemic treatment, and these have tended to become the predominant organisms in hospitals where the antibiotics are used. The penicillin-resistant staphylococci are penicillinase producers, and since such organisms cannot be obtained by subculture of sensitive organisms in the presence of the antibiotic, they are thought to have emerged by selection of pre-existing resistant strains. About 20 per cent of the staphylococci isolated from patients not in hospital are today resistant to penicillin, but a much higher proportion of resistant strains is found in hospital. Tetracycline-resistant staphylococci are now fairly common, and erythromycin resistance fluctuates with the degree to which the antibiotic is used. Chloramphenicol resistance is rare among staphylococci because it emerges less readily and because the antibiotic is nowadays not often used in hospital practice. Resistance of staphylococci to bacitracin and neomycin can be elicited *in vitro*, but does not appear in patients under treatment. Attempts to induce resistance of staphylococci to the new antibiotic vancomycin have been relatively unsuccessful.[30] Among the Gram-negative bacilli *Ps. pyocyanea* is exceptional in being uniformly sensitive to polymyxin, and in not acquiring resistance to that agent. The other coliform bacilli are variable in their sensitivity or resistance to the tetracyclines, chloramphenicol, polymyxin, and streptomycin; Proteus is always resistant to polymyxin. *M. tuberculosis* readily acquires resistance to streptomycin, isoniazid and P.A.S. Penicillin-resistant strains of clostridia and of actinomyces have been described, but are rare. As regards the antibiotics, streptomycin is unique in that all bacteria rapidly acquire resistance to it. Resistance to erythromycin and to novobiocin is acquired almost as rapidly by *Staph. aureus*.

The emergence of resistant variants presents a dilemma for which there is as yet no satisfactory answer. It is likely to be solved, in time, by the discovery of new agents for the treatment of infections by staphylococci, tubercle bacilli and coliforms, against which

emergence of resistant strains and for the return of symptoms after recovery must be made.

Nitrofurans. These compounds are active against a wide range of Gram-positive and Gram-negative organisms. Nitrofurantoin ("Furadantin")[72, 73] given by mouth (5 to 8 mg. per Kg. body weight daily, in 4 doses) has been found effective and free from severe toxicity in the treatment of urinary infections with Proteus and with *Bact. coli.*

Neomycin.[(26)] This antibiotic, produced by *Streptomyces fradiæ*, has bactericidal action against a wide range of Gram-positive and Gram-negative organisms, but like streptomycin has little or no activity against the clostridia, and is only moderately active against *Strep. pyogenes* and pneumococci. Neomycin resembles streptomycin in certain respects (including activity against *M. tuberculosis*), but in contrast with streptomycin it does not readily promote the emergence of resistant variants. Neomycin-resistant strains of *Staph. aureus* have rarely, if ever, been isolated from lesions treated with the agent.

Unfortunately, neomycin is liable to cause severe toxic action on the auditory nerve and on the kidneys, and is therefore unsuitable for systemic use. As it is not absorbed from the gut it can be given by mouth (1 gm. 4-hourly) for the destruction of fæcal flora before intestinal operations, and is probably the drug of choice in the treatment of infantile gastro-enteritis. It is also a valuable agent for treatment of superficial staphylococcal infections, for which purpose it is dispensed as a cream or an ointment containing 5 mg. per gm.

Bacitracin.[(26,28)] This is an antibiotic produced by a Gram-positive bacillus, and active against Gram-positive organisms, notably streptococci and staphylococci. Its use, like that of neomycin, is not associated with the emergence of resistant staphylococci.

Owing to its toxic action on the kidney, it is unsuitable for general systemic use, but newer purified preparations are considered safe enough to be given in very severe infections by staphylococci resistant to the other antibiotics. It has been used alone or together with neomycin in creams or ointments containing 500 units of bacitracin per gram, for the treatment of superficial infections with streptococci or staphylococci, and an aqueous solution has been used for the irrigation of infected pleura or peritoneum.

Other Chemotherapeutic Agents. Many agents in addition to those described above have been produced and some have been marketed. A few of these, including oleandomycin and spiramycin, resemble erythromycin in their mode of action, but the relationship between the members of this group is smaller than that between the tetracyclines. Other agents (e.g. gramicidin, the thiosemicarbazones and viomycin) are too toxic for systemic use.

The Problem of Resistance[(5,29,74)]

The problem of acquired resistance is of peculiar importance in surgery, for among the organisms most often involved are the staphylococci, the coliform bacilli and *M. tuberculosis*, all of which are exceptional for their resistance or their ability to produce resistant variants to most of the chemotherapeutic agents.

Resistant organisms may be defined as those which are able to grow in the presence of an agent at the concentrations which can be obtained with safety at the site of infection. For agents administered by the systemic routes, this concentration does not exceed the blood level unless they become concentrated in secretions (e.g. bile or urine). Higher

clinical assessment of agents should be used as the principal criterion of their value in treatment.

Methods of Administration

For most acute infections susceptible to chemotherapy a course of treatment with a single agent is adequate. Such a course should be short as a rule (e.g. 7 days), the dosage adequate and the route of administration appropriate (e g for very severe or fulminating infections very high dosage by the intravenous route is indicated; for ordinary acute infections intramuscular or oral routes are preferable).

For chronic or mixed infections and for some which respond poorly to single agents, the use of two or more agents together may be indicated. Such "combined chemotherapy" applied rationally has three valuable functions: (1) It delays the emergence of resistant variants (as in the treatment of tuberculosis with streptomycin and isoniazid or P.A.S.). (2) It may result in synergism or mutual potentiation (e.g. infection with *Strep. fæcalis* resistant to penicillin or streptomycin alone may respond to the two used in combination[31]); and (3) The range of action against a mixed flora may be increased by using two or more agents (e.g. infection of a burn with *Streptococcus pyogenes* and *Ps. pyocyanea* may successfully be treated by application of a mixture of penicillin and polymyxin, or by giving tetracycline by mouth and polymyxin locally). As *bactericidal* agents (e.g. penicillin, streptomycin, polymyxin, neomycin, bacitracin) act primarily against dividing cells, the simultaneous use of a predominantly *bacteriostatic* agent (e.g. the tetracyclines, chloramphenicol, erythromycin) is likely to interfere with the therapeutic action of the bactericidal drug. Evidence which suggests antagonism between the two groups of chemotherapeutic agents is supported by much *in vitro* experiment[32] and by at least one clinical study [33] When possible, therefore, it is advisable to avoid the combined use of bactericidal and bacteriostatic agents. True synergism has been claimed only in respect of mixtures of bactericidal agents, and can only be detected by tests of bactericidal power.

While it is usually desirable to give chemotherapy by the systemic routes, it is sometimes possible to achieve better results when the agent is applied locally. By this means a higher concentration of the drug can be brought in contact with the infective organisms, and interference by slough or fibrin can be overcome. Systemic chemotherapy may be used at the same time to supplement local therapy and to prevent invasion of uninfected tissues. Examples of local therapy include instillation of chemotherapeutic agents into pleural or peritoneal cavities, into joints, and into the cerebrospinal canal; oral administration of neomycin and other agents which are not absorbed, for elimination of organisms in the alimentary canal; and local applications of antibiotic creams or powders to burns.

Chemotherapy in Practice

Some applications of the principles outlined above are illustrated in the following notes on chemotherapy for particular surgical infections and on the indications for prophylaxis.

Osteomyelitis.[31,35,36,37,38] Before the advent of penicillin, incision through the periosteum was the routine procedure in the treatment of acute hæmatogenous osteomyelitis, but even if this operation was performed at an early stage, the prognosis was grave. When treated with penicillin, about 70 per cent of such infections diagnosed within 24 hours of onset resolve completely without the need for operation. Today penicillin is still the agent of choice, since most strains of *Staph. aureus* found outside hospitals (70–80 per

the organisms do not acquire resistance. Meanwhile steps must be taken (*a*) to delay the emergence of resistant strains, and (*b*) to prevent cross infection with such organisms. The former object may to some extent be achieved by (i) economy in the use of chemotherapy and especially in its prophylactic use; (ii) by avoiding the use of streptomycin when other agents can be used; (iii) by using two or more unrelated agents in combination; (iv) by using agents in rotation. The use of two or more agents at a time has been found particularly valuable in the treatment of tuberculosis; it depends on the principle that mutants are much less likely to emerge resistant to two unrelated agents at a time than to a single agent (or to two related agents such as "aureomycin" and "terramycin"). Unfortunately the method has severe limitations in treatment of wound infection, because of the imperfect control that antibiotics exert against many sensitive organisms in such cases. For that reason it may be desirable to use several agents in series, each for a short time only. The emergence of resistance is particularly menacing in the case of staphylococci, not only because they acquire resistance easily, but because they are carried in large numbers by many normal subjects. Cross infection is therefore common. The highest standard of asepsis in operating theatres, dressing stations and wards must be maintained in order to limit the spread of resistant organisms.

Indications for Chemotherapy and Selection of the Agent

The purpose of chemotherapy is to assist the body in overcoming infection. Before prescribing such treatment, therefore, the surgeon must decide that the natural defences cannot adequately cope with the invader, or at least that the good effects of treatment outweigh the risks of toxic action, sensitization or the appearance of resistant organisms. A boil or a small burn should usually not require chemotherapy, but unless the indications for chemotherapy are obvious, each case must be judged on its merits; chemotherapy would be needed for a small burn heavily colonized with *Strep. pyogenes*, or of a boil in the nostril, particularly in a patient liable to severe staphylococcal infections.

It is essential that the best drug or drugs should be used. A knowledge of the types of organism that cause particular infections and of their range of sensitivity makes it possible to start treatment with what is likely to prove the appropriate agent, even before the results of sensitivity tests are available; such prompt treatment may improve the prospects for chemotherapy, as organisms are more likely to be accessible to circulating antibiotics in the early stages of infection. In closed infections it may be necessary to dispense with bacteriological aids to treatment; whenever possible, however, specimens of the infected tissue—pus, exudate, blood or other material—should be examined for the presence of ærobic and anærobic organisms, which should be tested for sensitivity to the appropriate drugs. Follow-up specimens from the lesion should also be tested during and after treatment, so that the surgeon may know whether the organisms have persisted, and if so whether they have acquired resistance. When several alternative drugs are available, preference should be given to those with the smaller toxicity (e.g. penicillin) and those least likely (or unknown) to promote resistance. Even if the organism is sensitive to one or more antibiotics, it may be insusceptible to chemotherapy because of inadequate circulation (e.g. where there is pus, or slough, or a fibrin barrier); or the site may be one in which re-infection is likely (e.g. a decubitus ulcer or a fungating carcinoma). Sometimes, for no obvious reason, an antibiotic is found to be less—or more—effective in clinical use than sensitivity tests had led one to expect. It is therefore important that a

streptococci *in vitro*, by injection it is unsuccessful in removing them from the burn, probably because there is usually a mixed flora in the burn, including penicillinase producers. For such infections the tetracyclines[44] or, if these are inactive *in vitro*, erythromycin,[45] have been found highly successful in eliminating the streptococci. Recent studies suggest that combined therapy with novobiocin and erythromycin will eliminate sensitive staphylococci from burns treated by the closed method.[46] For infection with Gram-negative bacilli, systemic chemotherapy does not appear to reduce their growth on the burn, though it may prevent extensive invasion of the blood stream. Polymyxin applied locally (1 mg/gm. in a cream) has been found to eliminate *Ps. pyocyanea* from some burns,[47] and locally applied chloramphenicol appears to have a similar effect on *Strep. pyogenes* and *Staph. aureus*.[46, 48] The value of local application of chemotherapeutic agents to other open wounds is still a subject of controversy, but there is evidence to show that chloramphenicol applied to infected wounds can remove the resident organisms.[49]

Gas Gangrene.[50,51] Although penicillin is highly active against gas gangrene bacilli *in vitro*, it has been found to have little or no value in the treatment of gas gangrene unless the affected tissues are promptly and radically excised. Even where such an excision is made, the usefulness of penicillin is far from certain; but for obvious reasons it is desirable to give the antibiotic in high dosage (1 million units 3 or 4 hourly) for at least a week, and probably also to pack the wound after operation with an appropriate local chemotherapeutic agent (e.g. penicillin-sulphadimidine or penicillin-proflavine powder).

Tetanus. Destruction of tetanus bacilli is a minor part of the treatment for this disease. A course of penicillin G (1 million units a day by intramuscular injection) is recommended not only because of its expected action against the clostridia, but also as a prophylaxis against pneumonia. Local application to the open wound of penicillin powder or of zinc peroxide powder has been recommended, the latter being claimed to destroy the toxin as well as the organism of tetanus.[52]

Actinomycosis.[53,54,55,56,57] Most strains of *Actinomyces israeli* are sensitive to penicillin, which has proved very successful in curing infections with this organism. The drug should be given in high dosage for 4–6 weeks. Penicillin-resistant strains of the Actinomyces occur, and infection by them has been successfully treated with the tetracyclines, chloramphenicol and streptomycin. Stilbamidine has been found successful after a failure of other methods.

Urinary Infections.[58] Most chemotherapeutic agents are concentrated in the urine, and the choice of an agent should be dictated by the results of sensitivity tests. For *Bact. coli* or Proteus, the sulphonamides, the tetracyclines or chloramphenicol are generally chosen; the rational choice for *Ps. pyocyanea* is polymyxin; for *Strep. fæcalis*, a mixture of penicillin and streptomycin; and for *Staph. aureus*, penicillin, a tetracycline or erythromycin. Nitrofurantoin[72, 73] has been recommended, especially for infection with Proteus.

Unfortunately the good effects of treatment are liable to be transient in all but the mild and uncomplicated infections. Even when symptoms disappear, residual organisms are usually found in the urine, and recurrence is the rule when pyelonephritis is present, or urinary obstruction unrelieved. The use of antibiotics must never distract attention from the appropriate treatment of underlying causes.

Peritonitis. [illegible] the drugs of ch[illegible]

cent) are sensitive to penicillin. Early diagnosis and treatment are of the highest importance, and penicillin should be given in large dosage (e.g. 1–3 million units daily by intramuscular injection for 30 days). Blood culture and sensitivity tests on the organism isolated are valuable guides to treatment, but chemotherapy should not be delayed till the results are available. If there is no response after 24 hours treatment with penicillin, aspiration or incision is advisable, and exudate or pus obtained from the bone should be cultured. Another antibiotic may be indicated; the tetracyclines,[21] erythromycin,[23] and novobiocin[24] have all been used successfully in the treatment of osteomyelitis.

In chronic osteomyelitis pus, sequestra and an ischæmic barrier to penetration by systemic antibiotics interfere with treatment by chemotherapy, and resistant staphylococci and Gram-negative bacilli are likely to appear in the wound. The condition can still frequently be brought under control if the unhealthy and necrotic tissues can be adequately excised under cover of a suitable antibiotic screen. The role of chemotherapeutic dusting powder insufflated into the wound before closure is debatable. When viable tissues cannot be approximated it may be advisable to use chemotherapy by instillation into the depths through small tubes which can subsequently be removed.

Boils and Carbuncles. As in the case of acute osteomyelitis, the staphylococci which cause boils and carbuncles are usually sensitive to penicillin, though the incidence of resistant strains has increased in recent years. Chemotherapy is often unnecessary for boils, and is likely to be effective only if started very soon after symptoms appear. A sensitivity test on staphylococci from the nose may be valuable in the control of therapy, since pus is often not readily available. In the treatment of carbuncles, systemic chemotherapy is desirable and may, if started early, render operation unnecessary; often, however, it must be supported by drainage of abscesses or removal of slough. In the experience of Altemeir (1950)[37] penicillin has revolutionized the management of carbuncles, bringing both general and local manifestations under control within 48–72 hours.

Infections of the Hand.[39,40] *Staph. aureus* is nearly always the organism responsible for these infections. Pulp infections have been shown to heal more quickly after incision, and to be followed by fewer complications when penicillin is given.[40] Chemotherapy should be continued for one week, and for longer periods if complications (e.g. osteomyelitis) occur. Paronychia has been found to heal more quickly after drainage when penicillin is given; a single injection of benethamine penicillin has been found effective.[14] For tendon sheath infections systemic chemotherapy should be used as an ancillary measure to surgical treatment; penicillin G or another agent found active against the organisms cultured from the lesion should be given in large dosage and may also be instilled into the sheath.

Septicæmia and Pyæmia. Treatment depends on the results of blood culture, including sensitivity tests. Very high doses, given by the intramuscular or intravenous routes, are essential, and should be continued for 2 weeks after the patient becomes afebrile.[41] It is important that local sepsis from which the hæmatogenous infection originated should receive adequate treatment, including drainage and local chemotherapy. Septicæmia due to *Staph. aureus* and Gram-negative bacilli may fail to respond to treatment even when the organisms are sensitive;[42,43] this is probably due in most cases to failure in the removal of the local source of infection (e.g. extensive infected burns).

Infected Burns. *Strep. pyogenes* is still commonly found in burns, and causes more damage there than other organisms. Although penicillin is uniformly active against these

streptomycin and P.A.S. Lattimer and others[66] (1952) have reported successful treatment with drugs alone of a large series, including a number of patients with bilateral renal tuberculosis. They recommend 12 gm. of P.A.S. daily and 1 gm. of streptomycin every third day, the course being continued for a year or longer. For caseous lesions of one kidney, however, nephrectomy is desirable, and treatment with the appropriate chemotherapy minimizes the risks of extension. By accelerating scarring with contracture, chemotherapy may sometimes add to the damage caused by tuberculous infection.

In bone and joint tuberculosis, chemotherapy has improved the results of treatment when necrotic tissue is adequately curetted and abscesses are drained.

Prophylaxis. Chemotherapy has been used on a large scale in surgery for the protection of uncontaminated tissues against infection. With the gradual emergence of a resistant hospital flora, particularly of *Staph. aureus*, the sulphonamides, penicillin, and some of the newer antibiotics have lost a considerable part of their prophylactic and therapeutic value. The routine prophylactic use of antibiotics has therefore been criticized, and such criticism is reinforced by the known dangers of toxicity and by the risk that asepsis may be neglected if too much reliance is placed on chemoprophylaxis. It is therefore important to distinguish the genuine indications for prophylaxis from those situations in which it is unnecessary and potentially harmful.

There are three broad indications for prophylaxis:

(1) *Before Operations on the Large Intestine.* Sterilization of the gut contents has made it safe to resect and anastomose without a preliminary defunctioning colostomy. As a result, the fatality after resection of tumours of the colon has been greatly reduced. Phthalylsulphathiazole given for 3–5 days eliminates a large part of the fæcal flora, but a better result (often complete sterilization) may be obtained after a 24 hours' course of oral neomycin (1 gm. 4 hourly).[67] The administration of tetracycline with neomycin has also been recommended.

(2) *As an Aid to Asepsis during and after Certain Operations.*[68,69,70] Unlike preoperative sterilization of the gut, this is generally a true prophylaxis against organisms not already present at the operation site. It is, of course, recommended for the surgery of contaminated or infected areas; but also in patients with infection in parts of the body remote from the operation site, with indwelling catheters, with heart disease, or with lowered resistance to infection (e.g. in diabetes or agammaglobulinæmia); in operations on the brain, the lungs and the heart, and for emergency operations on extensive injuries. There is no evidence that chemotherapeutic cover has any beneficial effect after small clean operations, or even after such major procedures as nephrectomy or gastrectomy, though it may be considered desirable in such cases for the prevention of post-operative pneumonia. Procaine penicillin (300,000–600,000 units daily for 5 days) is commonly prescribed; it is a rational prophylaxis against streptococcal or pneumococcal infection, and against the anærobes, but it is unlikely to prevent staphylococcal sepsis. Tetracycline or chloramphenicol are more useful if the risks of infection are severe. In patients suffering from shock, intravenous injection of penicillin G or of tetracycline may be preferable. Even if they do not prevent infection, antibiotics may limit the spread of bacteria to healthy tissue. The reduced incidence of post-operative parotitis has been attributed to chemoprophylaxis.[71]

(3) *Prophylaxis of Open Wounds.* For extensive open wounds and for wounds contaminated with soil, street dirt, or fæces, systemic penicillin is a rational measure of

surviving after a course of oxytetracycline, the drug being given intravenously until oral administration became possible. Intraperitoneal oxytetracycline solution (2 mg. per ml.) has been found valuable.[60] The improved outlook for cases of peritonitis must be ascribed, at least in part, to chemotherapy.

Empyema.[61,62] The success of chemotherapy for pneumonia has led to a reduction in the incidence of empyema. Aspiration followed by the instillation of 500,000 units of penicillin every 2 or 3 days, together with systemic penicillin therapy, may lead to a complete recovery in early empyema. If the infection persists, however, and particularly when the pus is thick and fibrinous, open drainage following rib resection becomes necessary. The flora in empyema associated with pneumonia is usually sensitive to penicillin, but resistant organisms (especially staphylococci) may be found and the choice of treatment should then be changed in the light of sensitivity tests. The tetracyclines, erythromycin, chloramphenicol and novobiocin may be instilled into the pleural cavity, and also appear in the pleural exudate after systemic administration. Secondary infection with *Ps. pyocyanea* may be controlled by instillation of polymyxin.

Brain Abscess.[63,64,26] During the past 10 years there has been a considerable fall in the death rate from brain abscess. This is attributed in part to improved methods of diagnosis, but the use of antibiotics has undoubtedly played a major part in this improvement. Staphylococci, pneumococci and streptococci are the commonest infective agents; most of these are sensitive to penicillin, but resistant staphylococci are not uncommon. Complete recovery may occur after aspiration, followed by local instillation of penicillin (10,000 units) or bacitracin (10,000 units). A course of systemic penicillin should also be given, and some surgeons recommend intraventricular injection of the antibiotic (or antibiotics) to reduce the risks of a spread of infection to the meninges. The results of sensitivity tests on material aspirated from the abscess may indicate a change of treatment. A radio-opaque substance (thorotrast or diodone) injected with antibiotics into the abscess has been found to give useful information on the course of the disease.

Intensive and prolonged chemotherapy has been valuable also in the treatment of cavernous sinus thrombosis.[65]

Tuberculosis.[5] Streptomycin, P.A.S., and isoniazid have undoubtedly contributed much towards the reduced mortality from tuberculosis, and their value has been confirmed in a number of controlled trials. Tuberculosis is a generalized infection, and lesions appearing in bone or in the urinary tract are liable to be associated with pulmonary disease; treatment must be directed towards the elimination of the organisms from all foci. Chemotherapy is an important but ancillary component of this scheme, in which rest, diet and appropriate surgery are of primary importance.

Suggestions for courses of therapy and for the choice of two drugs to be used together are given above. Such treatment has the smallest effect on chronic fibrocaseous or fibrotic lesions, for which collapse therapy or lobectomy may be indicated. Chemotherapy during such operations reduces the danger of spreading the infection to healthy tissue, provided the organisms are still sensitive; operation should therefore not be unnecessarily delayed. Tuberculous lesions of the mouth, pharynx and larynx often resolve under systemic chemotherapy, and good results have also been reported in tuberculous enteritis and peritonitis. As such cases often respond well to conservative treatment, it is difficult to assess the part played by chemotherapy.

In tuberculosis of the kidney, the urine can be sterilized, at least temporarily, by

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TABLE I

ACTION OF CHEMOTHERAPEUTIC AGENTS ON SOME ORGANISMS OF IMPORTANCE IN SURGERY

Chemotherapeutic Agent	Strep Pyogenes	Staph Aureus	Bact. Coli	Klebsiella Group	Ps. Pyocyanea	Proteus Group	Cl. Tetani	Cl. Welchii	M. Tuberlosis	Actinomyces Israeli	Strep. Fæcalis
Sulphonamides	SR	sR	SR	SR	sR	SR	SR	SR	sR	SR	R
Penicillin	S^x	SR	R	R	R	sR	S	S(R)	R	S(R)	$(S)R^{\phi}$
Erythromycin	S	SR	R	R	R	R	S	S	R	s	SR
Novobiocin	S	S(R)	R	sR	R	SR	—	—	—	—	SR
Bacitracin	S	S	R	R	R	R	S	S	—	S	S
Tetracyclines	S(R)	SR	SR	SR	sR	SR	S	S	sR	S	(S)R
Chloramphenicol	s	S(R)	SR	SR	sR	SR	S	S	R	S	SR
Streptomycin	SR	SR	SR	SR	SR	SR	R	R	SR	S(R)	sR^{ϕ}
Neomycin	R	S	SR	SR	sR	SR	R	R	s	—	R
Polymyxin	R	R	SR	SR	S	R	R	R	R	R	R

Note: S = "All strains (or virtually all) sensitive." R = "All strains resistant." SR = "Sensitive and resistant strains occur, the latter including those which appear as the result of exposure to the agent." Brackets = "Rarely found." Small type = "Moderate sensitivity." x = "Therapeutic value somewhat diminished in mixed cultures with penicillinase-producing organisms". ϕ = "Combined therapy effective."

This table, compiled from various sources, is intended merely as a rough guide for clinical use. It is important that strains marked as "SR" should be tested for sensitivity on initial isolation and (if isolated) during the course of treatment.

TABLE II

ADMINISTRATION AND DOSAGE OF CHEMOTHERAPEUTIC AGENTS

Chemotherapeutic Agent	Average Adult Dosage: Oral	Parenteral	Intrathecal	Local
SULPHONAMIDES Sulphadimidine	3 g., then 1 g. 4- or 6-hourly	3 g., then 1 g. 4-hourly (10% solution i.v., 0·5% s.c.)	—	—
Sulphadiazine	3 g., then 1 g. 4- or 6-hourly	4 g., then 3 g. 12-hourly (i.v. or s.c.)	—	—
Sulphacetamide eyedrops	—	—	—	10% solution
Succinyl sulphathiazole	7 g., then 3·5 g. 4-hourly	—	—	—
PENICILLINS Sodium penicillin G	—	500,000 units 12-hourly i.m. (or i.v.)	10,000 units 12-hourly	Solutions: Creams 1,000 to 10,000 units per g.; Powder 10,000 units/g
Procaine penicillin	—	300,000–600,000 units daily i.m.	—	Solutions Creams 1,000 to 10,000 units per g.; Powder 10,000 units/g
Benzathine penicillin	—	600,000 units (1 dose i.m.) (often with procaine penicillin and penicillin G)	—	—
Benethamine penicillin	—	600,000 units (i.m. 1 dose)	—	—
Phenoxy-methyl penicillin	375 mg. daily (600,000 units) 3 doses per day	—	—	—
Penicillin ester	—	500,000 units 12-hourly	—	—
TETRACYCLINES Tetracycline ("Achromycin," "Tetracyn")	250 mg. 6-hourly	150 mg. 12-hourly i.m. 0·5 g. 12-hourly i.v. (1 mg. per ml. in i.v. fluid)	—	3% ointment 1% ophth ointment
Oxytetracycline ("Terramycin")	500 mg. 6-hourly	0·5–1·0 g. 12-hourly i.v. 0·5–1·0 g. daily i.m.	—	—
ERYTHROMYCIN ("Ilotycin," "Erythrocin")	300 mg. 6-hourly	1·0–2·0 g. daily i.v. (1 mg./ml. i.v. solution)	—	—
NOVOBIOCIN ("Albamycin," "Biotexin," "Cathomycin")	500 mg. 12-hourly	10 mg./kg. 6-hourly in i.v. fluids, 15–25 mg./kg. 12-hourly i.m.	—	—
CHLORAMPHENICOL ("Chloromycetin," "Alficetyn")	500 mg. 6-hourly	100 mg./kg. daily i.m. 50 mg./kg. daily i.v.	—	1% cream 5% solution 10% ear drops 1% eye ointment 5% dusting powder
STREPTOMYCIN	—	1·0 g. daily i.m.	100 mg. in 10 ml. saline	5% solution
POLYMYXIN B (OR E) ("Aerosporin")	500 mg. daily	2·5 mg./kg. daily i.m. (or 50 mg. 6- or 8-hourly)	5 mg. in 10 ml. saline daily	1 mg./g. cream 1 mg./ml. ear-drops or sub-conjunctival injection
NEOMYCIN	1 g. 4-hourly (pre-operation)	—	—	5 mg./g. or ml. in cream, ear and eye drops
BACITRACIN	20,000 units 4-hourly	40,000–80,000 units daily i.m. (for severe infection resistant to other agents only)	10,000 units daily	500–1,000 units per g. or per ml. in cream, ointments, solutions
NITROFURANTOIN ("Furadantin")	125 mg. 6-hourly	—	—	—

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